Exhibit 1

CURRICULUM VITAE **DAMIAN DARREN MEDICI**

Department of Orthopaedics Warren Alpert Medical School of Brown University 1 Hoppin Street, Coro West, Suite 402C

Tel: (401) 444-7180 Fax: (401) 444-5006

damian medici@brown.edu

EDUCATION

Undergraduate University of South Carolina, Biological Sciences,

Bachelor of Science, 2000

Graduate Harvard University, Biological Sciences, Doctor of

Philosophy, 2008

POSTGRADUATE TRAINING

Fellowship Beth Israel Deaconess Medical Center, Harvard

Medical School, Postdoctoral Fellow, Cancer

Biology, 2008-2009

POSTGRADUATE HONORS AND AWARDS

Dean's Scholar Award, Harvard University, 2008-2010 Travel Award, American Association of Anatomists, 2011 Distinguished Service Award, International FOP Association, 2011

ACADEMIC APPOINTMENTS

Instructor of Medicine, Harvard Medical School, 2009-2011
Instructor of Developmental Biology, Harvard School of Dental Medicine,
Harvard Medical School, 2011-2012

Assistant Professor of Orthopaedics, Warren Alpert Medical School of Brown University, 2012-

Assistant Professor of Medicine, Warren Alpert Medical School of Brown University, 2012-

HOSPITAL APPOINTMENTS

Instructor of Medicine, Beth Israel Deaconess Medical Center, 2009-2011 Director, Center for Regenerative Medicine, Rhode Island Hospital, 2012-Member, Cardiovascular Research Center, Rhode Island Hospital, 2012-Director, Orthopaedic Research Seminar Series, Rhode Island Hospital, 2013-

OTHER APPOINTMENTS

Ad hoc journal reviewer, 2005-

Nature Medicine, Journal of Clinical Investigation, Circulation Research, FASEB Journal, Kidney International, Journal of Pathology, American Journal of Pathology, Molecular Cancer Therapeutics, Bone, Developmental Dynamics, Matrix Biology, Laboratory Investigation, American Journal of Nephrology, Toxicology and Applied Pharmacology, Journal of Negative Results in Biomedicine, Acta Biochemica et Biophysica Sinica, Immunological Investigations, International Journal of Oral & Maxillofacial Surgery

Ad hoc grant reviewer, California Institute for Regenerative Medicine, 2013 Ad hoc grant reviewer, Vanderbilt University School of Medicine, Orthopaedic Surgery & Rehabilitation Pilot Grant Program, 2013

UNIVERSITY COMMITTEES

- Student Research Poster Evaluation Committee, Harvard School of Dental Medicine, 2010-2012
- Thesis Proposal Evaluation Committee, Victor Chiang: D.M.D. Candidate, Harvard School of Dental Medicine, 2011
- Thesis Defense Committee (Chair), Ilona Polur: D.M.D. Candidate, Harvard School of Dental Medicine, 2011
- Research Proposal Examination Committee, Mahshid Bahadoran: D.M.Sc. Candidate, Harvard School of Dental Medicine, 2011
- Research Proposal Examination Committee, Daliah Salem: D.M.Sc. Candidate, Harvard School of Dental Medicine, 2011
- Research Proposal Examination Committee, Anastasios Photopoulos: D.M.Sc. Candidate, Harvard School of Dental Medicine, 2012
- Research Proposal Examination Committee, Sharon Jin: D.M.Sc. Candidate, Harvard School of Dental Medicine, 2012

- Thesis Defense Committee, Jan-Renier Moonen, Ph.D. Candidate, University of Groningen, 2013
- Admissions Committee, Pathobiology Graduate Program, Brown University, 2013
- Thesis Defense Committee, Manisha Kanthilal, M.S. Candidate, Brown University, 2013

MEMBERSHIP IN SOCIETIES

American Society for Cell Biology, 2005-American Association for the Advancement of Science, 2009-The International Epithelial-Mesenchymal Transition Association, 2011-Orthopedic Research Society, 2014-

PUBLICATIONS LIST

ORIGINAL PUBLICATIONS IN PEER-REVIEWED JOURNALS

- 1. **Medici, D.**, Hay, E.D., and Goodenough, D.A. (2006). Cooperation between snail and LEF-1 transcription factors is essential for TGF-beta1-induced epithelial-mesenchymal transition. *Mol. Biol. Cell* 17, 1871-1879.
- 2. Nawshad, A., **Medici, D.**, Liu, C.C., and Hay, E.D. (2007). TGFbeta3 inhibits E-cadherin gene expression in palate medial-edge epithelial cells through a Smad2-Smad4-LEF1 transcription complex. *J. Cell Sci.* 120, 1646-1653.
- 3. **Medici, D.**, Razzaque, M.S., DeLuca, S., Rector, T.L., Hou, B., Kang, K., Goetz, R., Mohammadi, M., Kuro-o, M., Olsen, B.R., and Lanske, B. (2008). FGF-23-Klotho signaling stimulates proliferation and prevents vitamin D-induced apoptosis. *J. Cell Biol.* 182, 459-465.
- 4. **Medici, D.**, Hay, E.D., and Olsen, B.R. (2008). Snail and Slug promote epithelial-mesenchymal transition through beta-catenin-T-cell factor-4-dependent expression of transforming growth factor-beta3. *Mol. Biol. Cell* 19, 4875-4887.
- 5. Jinnin, M., Medici, D., Park, L., Limaye, N., Liu, Y., Boscolo, E., Bischoff, J., Vikkula, M., Boye, E., and Olsen, B.R. (2008).

- Suppressed NFAT-dependent VEGFR1 expression and constitutive VEGFR2 signaling in infantile hemangioma. *Nat. Med.* 14, 1236-1246.
- 6. **Medici, D.** and Nawshad, A. (2010). Type I collagen promotes epithelial-mesenchymal transition through ILK-dependent activation of NF-κB and LEF-1. *Matrix Biol.* 29, 161-165.
- 7. **Medici, D.**, Shore, E.M., Lounev, V., Kaplan, F.S., Kalluri, R., and Olsen, B.R. (2010). Conversion of vascular endothelial cells into multipotent stem-like cells. *Nat. Med.* 16, 1400-1406.
- 8. **Medici, D.**, Potenta, S., and Kalluri, R. (2011). TGF-beta2 promotes Snail-dependent endothelial-mesenchymal transition through convergence of Smad-dependent and Smad-independent signaling. *Biochem. J.* 437, 515-520.
- 9. Walsh, L.A., Nawshad, A., and **Medici, D.** (2011). Discoidin domain receptor 2 is a critical regulator of epithelial-mesenchymal transition. *Matrix Biol.* 30, 243-247.
- 10.Suh, N., Paul, S., Lee, H.J., Yoon, T., Shah, N., Son, A., Zhou, R., Reddi, A.H., **Medici, D.**, and Sporn, M.B. (2012). Synthetic triterpenoids, CDDO-imidazolide and CDDO-ethyl amide, induce chondrogenesis. *Osteoarthritis Cartilage* 20, 446-450.
- 11. **Medici, D.** and Olsen, B.R. (2012). Rapamycin inhibits proliferation of hemangioma endothelial cells by reducing HIF-1-dependent expression of VEGF. *PLoS One* 7, e42913.

OTHER PEER-REVIEWED PUBLICATIONS

- 1. Kizu, A., **Medici, D.**, and Kalluri, R. (2009). Endothelial-mesenchymal transition as a novel mechanism for generating myofibroblasts during diabetic nephropathy. *Am. J. Pathol.* 175, 1371-1373.
- 2. **Medici, D.** and Olsen, B.R. (2011). Transforming blood vessels into bone. *Cell Cycle* 10, 362-363.

- 3. **Medici, D.** and Olsen, B.R. (2012). The role of endothelial-mesenchymal transition in heterotopic ossification. *J. Bone Miner. Res.* 27, 1619-1622.
- 4. **Medici, D.** and Kalluri, R. (2012). Endothelial-mesenchymal transition and its contribution to the emergence of stem cell phenotype. *Semin. Cancer Biol.* 22, 379-384.
- 5. Susienka, M. and **Medici**, **D.** (2013). Vascular endothelium as a novel source of stem cells for bioengineering. *Biomatter* 3, e24647.
- 6. Ramirez, D.M., Ramirez, M.R., Reginato, A.M., and **Medici, D.** (2014). Molecular and cellular mechanisms of heterotopic ossification. *Histol. Histopathol.* (In Press)
- 7. Gonzalez, D. and **Medici, D.** (2014). Signaling mechanisms of epithelial-mesenchymal transition. *Sci. Signal*. (In Press)

BOOKS AND BOOK CHAPTERS

- 1. **Medici, D.** (2008). Pathogenetic Mechanisms of Hemangioma Endothelial Cells. *Harvard University Archives*. Harvard University Press. (Thesis)
- 2. Medici, D. and Olsen, B.R. (2012). Transformation of Vascular Endothelial Cells into Multipotent Stem-Like Cells: Role of the Activin-Like Kinase-2 Receptor. Stem Cells and Cancer Stem Cells: Therapeutic Applications in Disease and Injury. Springer. Volume 8, Chapter 19.

MANUSCRIPTS SUBMITTED OR IN PREPARATION

- 1. Walsh, L.A., Ramirez, D., Ramirez, M., Mulliken, J.B., and **Medici, D.** Endothelial-mesenchymal transition promotes the natural regression of infantile hemangiomas. (Submitted)
- 2. Khan, Z., Ramirez, M., Ramirez, D., Mulliken, J.B., and **Medici, D.** Proliferation of infantile hemangiomas induced by hepatocyte growth factor expression from the tumor stroma. (Submitted).

- 3. Jorna, L., Ramirez, M., Ramirez, D., Susienka, M.J., Liang, O.D., Mulliken, J.B., Krenning, G., and **Medici, D.** ERK5 regulates the proliferation and survival of hemangioma endothelial cells. (Submitted)
- 4. Tsinkalovsky, O., Kuznetsov, S., Cherman, N., Susienka, M.J., Shore, E.M., Robey, P.G., and **Medici, D.** Generation of endochondral bone from vascular endothelial cells in hydroxyapatite/tricalcium phosphate microparticle transplants. (In preparation).
- 5. Servais, J.M., Liang, O.D., Ramirez, D., Ramirez, M., Taylor, H., Sullivan, S., Mulliken, J.B., Huang, S., and **Medici, D.** Bevacizumab inhibits hemangioma proliferation and associated hypothyroidism. (In preparation)

ABSTRACTS

- 1. **Medici, D.**, Sitara, D., DeLuca, S., Mohammadi, M., Kuro-o, M., Razzaque, M.S., Olsen, B.R., Erben, R.G., and Lanske, B. (2008). FGF-23: Beyond Pi regulation. *Calcified Tissue Int.*, ECTS 35th European Symposium on Calcified Tissue, Barcelona, Spain
- 2. **Medici, D.**, Shore, E.M., Kaplan, F.S., Kalluri, R., and Olsen, B.R. (2009). Vascular endothelial transdifferentiation to multipotent stemlike cells. Gordon Research Conference: Cartilage Biology and Pathology, Les Diablerets, Switzerland
- 3. **Medici, D.**, Shore, E.M., Lounev, V., Kaplan, F.S., Kalluri, R., and Olsen, B.R. (2011). Role of endothelial-mesenchymal transition in heterotopic ossification. Keystone Symposia on Molecular and Cellular Biology: Epithelial Plasticity and Epithelial to Mesenchymal Transition, Vancouver, BC, Canada
- 4. **Medici, D.**, Shore, E.M., Lounev, V., Kaplan, F.S., Kalluri, R., and Olsen, B.R. (2011). Role of endothelial-derived stem cells in human disease. Gordon Research Conference: Angiogenesis, Newport, RI
- 5. Li, Y.F., Li, Y., Xu, L., Servais, J.M., Frank, E., Lazarev, A., Olsen, B.R., Grodzinski, A.J., and **Medici, D.** (2011). Mechanical stress-induced TGF-β1 expression mediates HTRA1/DDR2 associated

- degradation of articular cartilage matrix. *J. Orthopaedic Res.* Orthopaedic Research Society 57th Annual Meeting, Long Beach, CA
- 6. Walsh, L.A., Mulliken, J.B., and **Medici, D.** (2011). Role of endothelial-mesenchymal transition in hemangioma regression. 5th International Epithelial-Mesenchymal Transition Meeting, Biopolis, Singapore
- 7. Walsh, L.A., Mulliken, J.B., and **Medici, D.** (2012). Endothelial-mesenchymal transition promotes the natural regression of infantile hemangiomas. 17th Annual International Vascular Biology Meeting, Wiesbaden, Germany
- 8. Walsh, L.A., Mulliken, J.B., and **Medici, D.** (2012). Endothelial-mesenchymal transition promotes the natural regression of infantile hemangiomas. Gordon Research Conference: Endothelial Cell Phenotypes in Health and Disease, Lucca, Italy
- 9. Walsh, L.A., Ramirez, D., Ramirez, M., Mulliken, J.B., and **Medici**, **D.** (2013). Endothelial-mesenchymal transition promotes the natural regression of infantile hemangiomas. FASEB Scientific Research Conference, The TGF-β Superfamily: Signaling in Development and Disease, Steamboat Springs, CO
- 10. Susienka, M.J., Ramirez, M., Ramirez, D., Spangler, T., Gonzalez, D., Liang, O.D., and **Medici, D.** (2013). Endothelial-mesenchymal transition as a novel mechanism for tissue regeneration. 6th International Epithelial-Mesenchymal Transition Meeting, Alicante, Spain
- 11. Susienka, M.J., Walsh, L.A., Liang, O.D., and **Medici, D.** (2014). Identifying the molecular mechansims by which synthetic triterpenoids induce chondrogenesis. *J. Orthopaedic Res.* Orthopaedic Research Society 60th Annual Meeting, New Orleans, LA
- 12. Susienka, M.J., Ramirez, M., Ramirez, D., Spangler, T., Gonzalez, D., Liang, O.D., and **Medici, D.** (2014). Endothelial-mesenchymal transition as a novel mechanism for tissue regeneration. 18th International Vascular Biology Meeting, Kyoto, Japan

INVITED PRESENTATIONS

- 1. Mechanisms of Type I Collagen-induced Epithelial-Mensenchymal Transition, Department of Oral Medicine, Infection & Immunity, Harvard School of Dental Medicine, 2008, Regional
- 2. Vascular Endothelial Transdifferentiation to Multipotent Stem-like Cells, Gordon Research Conference: Cartilage Biology and Pathology, Les Diablerets, Switzerland, 2009, International
- 3. Molecular Pathogenesis of Infantile Hemangioma, Department of Oral Biology, University of Nebraska Medical Center, Lincoln, NE, 2010, National
- 4. Disease Process Reveals New Source of Stem Cells, Dean's Town Meeting, Harvard School of Dental Medicine, 2010, Regional
- 5. Endothelial Plasticity in Human Disease, Vascular Anomalies Seminar Series, Harvard School of Dental Medicine/Children's Hospital Boston, 2010, Regional
- 6. Role of Endothelial-Mesenchymal Transition in Heterotopic Ossification, Keystone Symposia on Molecular and Cellular Biology: Epithelial Plasticity and Epithelial to Mesenchymal Transition, Vancouver, BC, Canada, 2011, International
- 7. Transforming Blood Vessels into Bone, Grand Rounds, Department of Oral and Maxillofacial Surgery, Massachusetts General Hospital, 2011, Regional
- 8. Endothelial-Derived Stem Cells in Human Disease, Vascular Biology Seminar Series, Department of Pathology, Brigham & Women's Hospital, 2011, Regional
- 9. Molecular Mechanisms of Hemangioma Progression, Symposium on Extracellular Matrix in Health and Disease, Harvard Medical School, 2011, Regional

- 10. Endothelial Origin of Ectopic Bone. Bone Research Seminar Series, Harvard Medical School/Massachusetts General Hospital, 2011 Regional
- 11. Transforming Blood Vessels into Bone, Hospital for Special Surgery, New York, NY, 2011, National
- 12. Endothelial Cell Plasticity in Human Disease, Department of Pharmacology and Systems Therapeutics, Mount Sinai School of Medicine, New York, NY, 2011, National
- 13. Endothelial Cell Plasticity in Heterotopic Ossification, Scientific Workshop: Strategies for the Treatment of FOP, International Fibrodysplasia Ossificans Progressiva Association, University of Pennsylvania School of Medicine, Philadelphia, PA, 2011, National
- 14. Vascular Origin of Heterotopic Bone, Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA, 2011, National
- 15. Endothelial-Derived Stem Cells in Human Disease, Gordon Research Conference: Angiogenesis, Newport, RI, 2011, National
- 16.BMP Signaling in Heterotopic Ossification, Seminar Series on Bone Morphogenetic Proteins, Harvard Medical School, 2011, Regional
- 17. Endothelial-Derived Stem Cells in Human Disease, Department of Pharmacology and Toxicology, Dartmouth Medical School, Hanover, NH, 2011, National
- 18. Transforming Blood Vessels into Bone, Musculoskeletal Research Seminar Series, Department of Orthopedic Surgery, Washington University School of Medicine, St. Louis, MO, 2011, National
- 19. Molecular and Cellular Mechanisms of Hemangioma Involution, Department of Pathology and Medical Biology, University of Groningen, Groningen, The Netherlands, 2012, International

- 20. Transforming Blood Vessels into Bone, Orthopaedic Research Seminar, Rhode Island Hospital, Warren Alpert Medical School of Brown University, Providence, RI, 2012, Regional
- 21.Endothelial-Mesenchymal Transition Promotes the Natural Regression of Infantile Hemangiomas, 17th Annual International Vascular Biology Meeting, Wiesbaden, Germany, 2012, International
- 22. Mechanisms of Heterotopic Ossification, Orthopaedic Research Meeting, Rhode Island Hospital, Providence, RI, 2012, Regional
- 23. Endothelial-Derived Stem Cells in Human Disease, Faculty on Parade Seminar, Pathobiology Program, Brown University, Providence, RI, 2012, Regional
- 24. Endothelial-Derived Stem Cells in Human Disease, Cardiovascular Research Center Seminar Series, Rhode Island Hospital, Providence, RI, 2012, Regional
- 25. Endothelial-Derived Stem Cells in Human Disease, Pulmonary Research Conference, Brown University/Rhode Island Hospital, Providence, RI, 2013, Regional
- 26. Endothelial-Derived Stem Cells in Human Disease, Pathobiology Seminar Series, Brown University, Providence, RI, 2013, Regional
- 27. Endothelial-Derived Stem Cells in Human Disease, Pulmonary Medicine Seminar Series, Providence VA Medical Center, Providence, RI, 2013, Regional
- 28. Mechanisms of Heterotopic Ossification, External Advisory Committee Meeting, COBRE for Skeletal Health and Repair, Rhode Island Hospital, Providence, RI, 2013, Regional
- 29. Pathogenesis of Infantile Hemangioma, Pediatric Research Conference, Women & Infants Hospital, Providence, RI, 2013, Regional

- 30. Pathogenesis of Infantile Hemangioma, Division of Hematology/Oncology Seminar, Rhode Island Hospital, Providence, RI, 2013, Regional
- 31. Endothelial-Derived Stem Cells in Disease and Tissue Regeneration, Department of Molecular Pharmacology, Physiology & Biotechnology, Brown University, Providence, RI, 2013, Regional
- 32. Endothelial-Mesenchymal Transition Promotes the Natural Regression of Infantile Hemangiomas, FASEB Scientific Research Conference, The TGF-β Superfamily: Signaling in Development and Disease, Steamboat Springs, CO, 2013, National
- 33. Endothelial-Mesenchymal Transition for Musculoskeletal Tissue Regeneration, Orthopaedic Research Meeting, Rhode Island Hospital, Providence, RI, 2013, Regional
- 34. Endothelial-Mesenchymal Transition as a Novel Mechanism for Tissue Regeneration, 6th TEMTIA Meeting, Alicante, Spain, 2013, International
- 35. Pathogenesis of Infantile Hemangioma, Cardiovascular Research Center, Massachusetts General Hospital, Boston, MA, 2013, Regional
- 36.Endothelial-Derived Stem Cells for Tissue Engineering and Regeneration. Biomedical Engineering Seminar Series, Center for Biomedical Engineering, Brown University, 2014, Regional
- 37. Endothelial-Mesenchymal Transition as a Novel Mechanism for Tissue Regeneration, 18th International Vascular Biology Meeting, Kyoto, Japan, 2014, International
- 38.Endothelial-Mesenchymal Transition as a Novel Mechanism for Tissue Regeneration, Yale Cardiovascular Research Center/North American Vascular Biology Organization Meeting, Cardiovascular Inflammation and Remodeling Symposium, New Haven, CT, 2014, Regional

GRANTS

- 1. Molecular and Cellular Mechanisms of Hemangioma Progression, The John Butler Mulliken Foundation, 2011-2014, Principal Investigator, \$99,100
- 2. Endothelial Plasticity in Human Disease (R01HL112860), National Institutes of Health: National Heart, Lung and Blood Institute, 2012-2017, Principal Investigator, \$1,990,600
- 3. Mechanisms of Heterotopic Ossification (P20GM104937), National Institutes of Health: National Institute of General Medical Sciences, 2012-2017, Investigator/Project Leader, \$1,000,000

UNIVERSITY TEACHING ROLES

Courses

- CB300: Advanced Topics in Cell, Molecular and Developmental Biology, Harvard Medical School, Teaching Assistant, 2005
- IDP602: Introduction to Research: Research Methodology in the Biomedical Sciences, Harvard School of Dental Medicine, Instructor, 2010-2012
- OB612: Autoimmune Diseases, Harvard School of Dental Medicine, Instructor, 2010-2012
- OB613: Mechanisms of Cancer Progression, Harvard School of Dental Medicine, Course Director, 2010-2012
- OB606: Stem Cells and Tissue Regeneration, Harvard School of Dental Medicine, Instructor, 2011-2012
- OB617: Bone Development and Disease, Harvard School of Dental Medicine, Instructor, 2011-2012
- ENGN2910S: Cancer Nanotechnology, Brown University, Lecturer, 2014

Laboratory Supervision and Training

- Scott Potenta, M.D., Ph.D Student: Harvard Medical School, 2008-2009 Illana Stanley, Ph.D. Student: Harvard University, 2008-2010
- Akane Kizu, M.D., Postdoctoral Fellow: Harvard Medical School, 2008-2010
- Logan Walsh, Ph.D. Student: University of Western Ontario, Visiting Fellow: Harvard Medical School, 2009
- Aika Okazawa, M.D. Student: Okayama Medical University, Visiting Fellow: Harvard Medical School, 2010-2011

Kai Hu, Ph.D. Student: Harvard University, 2010-2011

Logan Walsh, Ph.D., Postdoctoral Fellow: Harvard Medical School, 2010-2012

Oleg Tsinkalovsky, M.D., Postdoctoral Fellow: Harvard Medical School, 2010-2012

Zainab Khan, D.M.Sc., Postdoctoral Fellow: Harvard School of Dental Medicine/Harvard Medical School, 2011-2012

Jacqueline Servais, D.M.D. Student: Tufts University, Visiting Fellow: Harvard School of Dental Medicine/Harvard Medical School, 2012

George Jiao, B.S. Student: Boston University, Visiting Fellow: Harvard School of Dental Medicine/Harvard Medical School, 2012

Lysanne Jorna, M.S. Student: University of Groningen, Visiting Fellow: Brown University, 2012-2013

Michael Susienka, Ph.D. Student: Brown University, 2012-

Travis Spangler, M.D. Student: Brown University, 2012-

Nelly Valkov, Ph.D. Student: Brown University, 2013

Emma Flaherty, Ph.D. Student: Brown University, 2013

David Gonzalez, B.S. Student: Brown University, 2013-

Adam Dreisman, M.D. Student: Brown University, 2013-

Cheri Liu, Ph.D. Student: Brown University, 2013

Susan Leggett, Ph.D. Student: Brown University, 2013-2014

Agnieszka Blazejczyk, Ph.D. Student: Polish Academy of Sciences, Visiting Fellow: Brown University, 2013-2014

Carlota Pereda Serras, B.S. Student: Brown University, 2014-

HOSPITAL TEACHING ROLES

Courses

Genetic Basis of Musculoskeletal Disorders, Orthopaedic Basic Science, Rhode Island Hospital, Lecturer, 2012

Bone Forming Diseases and Spondyloarthropathies, Orthopaedic Basic Science, Rhode Island Hospital, Lecturer, 2014

Laboratory Supervision and Training

Diana Ramirez, B.S., Research Assistant, Rhode Island Hospital, 2012-Melissa Ramirez, B.S., Research Assistant, Rhode Island Hospital, 2012-

Olin Liang, Ph.D., Postdoctoral Fellow, Rhode Island Hospital, 2013-

Exhibit 2

September 9, 2015

By Overnight Mail and Email (chale@toddweld.com)

Damian Medici, Ph.D

c/o Corrina L. Hale, Esq.

Todd & Weld LLP

One Federal Street

Boston, MA 02110

593 Eddy Street Providence, RI 02903 Te¹ 401 444-5337

Fax 401 444-8161

Dear Dr. Medici:

In light of Lifespan Corporation's decision to uphold the findings of research misconduct articulated in the Final Report of the Lifespan Investigation Committee, Rhode Island Hospital has made a decision to terminate your employment with the Hospital in accordance with the termination-for-cause provisions in your contract. This letter provides you with notice of such termination, which will become effective on September 24, 2015. The summary below describes the benefits you will receive following your last day of employment.

As a participant in Lifespan's Benefits Program, your coverage will be affected as follows:

Health Insurance Benefits: Your existing medical coverage will end on September 30, 2015. However you will be able to continue coverage under COBRA. We will subsidize the COBRA rate so that you can continue at the current active employee contribution rate for a period of one (1) month following your last day of employment, meaning that our subsidy will begin on October 1, 2015 and end on October 31, 2015. You will receive two letters from Benefit Strategies. The first is a COBRA notice informing you of your rights under COBRA and the total cost for your insurance under COBRA. You will also receive a separate letter from Benefit Strategies which details the subsidy for the one month period. In order to maintain your coverage under COBRA you must elect coverage under COBRA and return the form to Benefit Strategies. You will make your payments to Benefit Strategies directly. Coverage will not be reinstated until you have made payment to Benefit Strategies. If you have any questions regarding the amount to remit or your election you should contact Benefit Strategies directly at 888 401-3539.

Life Insurance and Long-term Disability Insurance: Coverage will end on your last day of work. Optional conversion information, if available, will be mailed to your home.

Retirement: A statement of your benefits under this program will be forwarded to you within three months. Please call 401-444-6337 if you have questions regarding your retirement benefits.

<u>Tax-Sheltered Annuities [403(b) Plans]</u>: Contributions you may have made under a salary reduction agreement will cease as of your last regular pay. If you would like additional information on the status of your account(s), please contact the Benefits Office at 401-444-5265.

Vacation/Holiday Hours: You will receive pay for all accrued and unused vacation and holiday hours which will be paid to you in a separate check in the pay period following your last day of employment. Accruals end on the last day of active employment.

Coastline Employee Assistance Program (EAP): The services of Coastline Employee Assistance Program will continue to be available to you for eighteen months following your last day of employment. You may contact Coastline EAP at any time you or your family members desire their services. Information regarding Coastline EAP is enclosed. If you have any questions concerning the preceding information, please feel free to contact the

Benefits Office at 401-444-5265.

Sincerely,

Louis J. Sperling

Vice President of Human Resources

Lifespan Corporation

Lifespan

10 September, 2015

Michael Ehrlich, M.D.
Chief, Department of Orthopedics
Rhode Island Hospital
2 Dudley Street
Providence, Rhode Island 02905

CONFIDENTIAL

Re: Damian Medici, Ph.D.

Dear Dr. Ehrlich:

As you know, over the course of the past year, an Investigation Committee comprised of Dr. Medici's peers was charged by Lifespan to investigate certain allegations of research misconduct that were brought forward. In its Final Report dated 18 August 2015, the Investigation Committee found that Dr. Medici committed research misconduct in connection with three allegations. This decision was affirmed in its entirety by Dr. John Murphy, the Deciding Official at Lifespan. As required by Federal law, Lifespan reported this decision to the Office of Research Integrity at the U.S. Department of Health and Human Services. Additionally, as a consequence of these findings, Rhode Island Hospital made a decision to terminate Dr. Medici effective 24 September 2015.

I am available to discuss the above if you wish, but please be advised that any such discussion would be limited by the rules of confidentiality governing the entire proceedings.

Very truly yours,

Peter J. Snyder, Ph.D.

Sr. Vice President & Chief Research Officer,

865 Sh

Research Integrity Officer

Lifespan Corporation

cc: John B. Murphy, M.D.

Kenneth E. Arnold, Esq.

Therese F. Eckford, Esq.



Peter J. Snyder, PhD Senior Vice President and

Chief Research Officer

Research Administration

Department of Neurology The Warren Alpert Medical School of Brown University

1st Floor, Suite 1.001 Providence, RI 02903

Tel 401 444-4117 Email psnyder@lifespan.org

Adjunct Professor Child Study Center Yale University School of

Senior Associate Editor.

The Journal of the Alzheimer's Association

Alzheimer's & Dementia:

Coro West One Hoppin Street

Professor

Medicine

Lifespan

10 September, 2015

Jack A. Elias, M.D., Dean Alpert Medical School of Brown University 91 Waterman Street Providence, RI 02912

CONFIDENTIAL

Re: Damian Medici, Ph.D.

Dear Dean Elias:

I am writing in my capacity as the Research Integrity Officer of Lifespan Corporation and in light of the fact that Dr. Medici has held dual appointments at Lifespan and at Brown.

Over the course of the past year, an Investigation Committee comprised of Dr. Medici's peers was charged by Lifespan to investigate certain allegations of research misconduct that were brought forward. In its Final Report dated 18 August 2015, the Investigation Committee found that Dr. Medici committed research misconduct in connection with three allegations. This decision was affirmed in its entirety by Dr. John Murphy, the Deciding Official at Lifespan. As required by Federal law, Lifespan reported this decision to the Office of Research Integrity at the U.S. Department of Health and Human Services. Additionally, as a consequence of these findings, Rhode Island Hospital made a decision to terminate Dr. Medici effective 24 September 2015.

I am available to discuss the above if you wish, but please be advised that any such discussion would be limited by the rules of confidentiality governing the entire proceedings.

Very truly yours,

Peter J. Snyder, Ph.D.

Sr. Vice President & Chief Research Officer,

DL-92-

Research Integrity Officer

Lifespan Corporation

cc: John B. Murphy, M.D.

Kenneth E. Arnold, Esq.

Therese F. Eckford, Esq.



Peter J. Snyder, PhD Senior Vice President and

Chief Research Officer

Research Administration

Department of Neurology The Warren Alpert Medical

School of Brown University

Coro West One Hoppin Street 1st Floor, Suite 1.001 Providence, RI 02903

Professor

Medicine

Tel 401 444-4117 Email psnyder@lifespan.org

Adjunct Professor

Child Study Center Yale University School of

Senior Associate Editor,

Alzheimer's Association

Alzheimer's & Dementia: The Journal of the

Exhibit 3

Final Report
of the
Lifespan
Investigation Committee

In the Matter of

Damian Medici, Ph.D.

Jonathan Kurtis, M.D., Ph.D. (Chair) Adam Chodobski, Ph.D. Loren D. Fast, Ph.D. Bharat Ramratnam, M.D.

August 18, 2015

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<u>APPENDIX I</u>: APPENDIX OF EXHIBITS TO FINAL REPORT (Exhibits numbered 1 through 51)

<u>APPENDIX II [separate binder]</u>: DR. DAMIAN MEDICI'S RESPONSE TO THE LIFESPAN INVESTIGATION COMMITTEE (with Exhibits designated A through PP)

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I. INTRODUCTION

This report was prepared by the Lifespan Investigation Committee convened to look into allegations that Damian Medici, Ph.D., ("Dr. Medici" or the "Respondent") engaged in various forms of research misconduct in his capacities as an employee of Rhode Island Hospital, Inc., and a principal investigator on diverse research projects. The investigation has been carried out in accordance with the provisions of 42 C.F.R. Part 93 ("Public Health Service Policies on Research Misconduct") and the Lifespan Policy on Research Misconduct, a copy of which appears as Exhibit 1 in the Appendix of Exhibits that accompanies this report. The Investigation Committee consists of the following individuals: Jonathan Kurtis, M.D., Ph.D., Professor of Pathology and Laboratory Medicine at the Alpert Medical School of Brown University and Director of the Lifespan Center for International Health Research, who chaired the Committee; Adam Chodobski, Ph.D., Associate Professor of Emergency Medicine (Research) at the Alpert Medical School of Brown University and member of the Department of Emergency Medicine at Rhode Island Hospital; Loren D. Fast, Ph.D., Associate Professor of Medicine (Research) at the Alpert Medical School of Brown University and member of the Division of Hematology/Oncology at Rhode Island Hospital; and Bharat Ramratnam, M.D. Associate Professor of Medicine at the Alpert Medical School of Brown University and Director of the COBRE Center for Cancer Research Development at Rhode Island Hospital

The federal regulations cited above apply to all four of the reviewed allegations of research misconduct because Dr. Medici, in addition to deriving research support from private sources, was supported at all times pertinent to this matter by Public Health Service funds. Specifically, he received PHS support from the following grants:

- 1) National Institute of General Medical Sciences Award #5P20GM104937-07 (COBRE Project 3, "Mechanisms of Heterotopic Ossification"); and
- 2) National Heart, Lung and Blood Institute Award #5R01HL112860-04 ("Endothelial Plasticity in Human Disease").

II. SUMMARY OF FINDINGS

After a comprehensive investigation, the Investigation Committee made the following findings concerning the four allegations:

1) With respect to <u>Allegation 1</u> (set out in full in Part VII.A), the Investigation Committee found by a preponderance of the evidence that Dr. Medici intentionally falsified immunoblotting images in a manuscript submitted for publication, thereby committing research misconduct.

Hereafter, exhibits will be cited by the notation "<u>Ex.</u>" followed by a page reference where applicable. In the case of transcripts from the interviews of witnesses, the citation will also note the name of the witness in brackets, as in the following format: "<u>Ex.</u>___, p.__ [witness name]." Where cited witness testimony includes material edits submitted as errata, the citation indicates "as amended".

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- 2) With respect to <u>Allegation 2</u> (set out in full in Part VII.B), the Investigation Committee found by a preponderance of the evidence that Dr. Medici intentionally falsified morphological images in a manuscript submitted for publication, thereby committing research misconduct.
- 3) With respect to <u>Allegation 3</u> (set out in full in Part VII.C), the Investigation Committee found that the evidence was insufficient to support a finding of research misconduct.
- 4) With respect to <u>Allegation 4</u> (set out in full in Part VII.D), the Investigation Committee found by a preponderance of the evidence that Dr. Medici intentionally falsified and/or fabricated data by manipulating live cell cultures in the course of research experiments, thereby committing research misconduct.

The Investigation Committee's detailed factual findings and analyses are discussed below.

III. GENERAL FACTUAL BACKGROUND

The Respondent in this matter, Dr. Medici, received his Ph.D. in Biological Sciences in 2008 from Harvard University, where he worked in the laboratory of Dr. Bjorn Olsen at the Harvard School of Dental Medicine (HSDM) and Harvard Medical School (HMS). He did postdoctoral training in labs at HMS and Beth Israel Deaconess Medical Center. He held instructorships at HMS and HSDM from 2009 to 2012. Dr. Medici joined the staff of Rhode Island Hospital, one of the affiliate hospitals of Lifespan Corporation, Inc., and joined the faculty of the Warren Alpert Medical School at Brown University as an Assistant Professor of Orthopaedics in the late summer of 2012. (Ex. 2; Ex. 3A, p. 14 [Medici].)

Dr. Medici's research explores endothelial cell plasticity, the role of endothelial cell transitions to stem cell-like cells in human disease processes, and the potential for generating human tissues from such transitions. While at Harvard, Dr. Medici co-authored several manuscripts accepted for publication in scientific journals reporting research into, or incorporating, techniques for transitioning endothelial cells to mesenchymal cells. At Rhode Island Hospital, various members of his lab continued to perform research involving endothelial-mesenchymal transition (EndMT) and using various types of human endothelial cells, including human dermal microvascular endothelial cells (HDMECs), a type of cell with which Dr. Medici had not previously attempted EndMT.

In September 2012, Dr. Medici accepted Michael Susienka, a second-year graduate student, to train in his lab. Mr. Susienka's research project involved chondrogenesis, the process of cartilage formation. As part of his research he attempted to induce EndMT with the use of various chemicals (bone morphogenic protein 2, or BMP2, and various triturpenoids). Despite a number of attempts over the course of a year, Mr. Susienka never succeeded in inducing EndMT. (Ex. 3B, pp. 12-13 [Susienka].) Several other members of Dr. Medici's lab, working with the

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same or other endothelial cell types and with the same or other transforming agents, also experienced difficulty achieving EndMT. (<u>Id.</u> at 13-15; <u>Ex.</u> 3C, pp. 7-9 [M. Ramirez]; <u>Ex.</u> 3D, pp. 9-10 [D. Ramirez]; <u>Ex.</u> 3E, p. 17 [Valkov]; <u>Ex.</u> 3F, pp. 7-12 [Spangler].)

In the summer of 2013, Mr. Susienka turned his attention to preparing a dissertation proposal in connection with his departmental qualifying exam. In consultation with Dr. Medici, he developed a proposal to test the hypothesis that EndMT plays a role in the regeneration of skeletal tissue. Dr. Medici provided him with a preliminary outline for his proposal, including some figures of Western blots and cell morphology images for cells purportedly treated with triturpenoids. (Ex. 4.) Working with the outline, Mr. Susienka developed his qualifying exam research proposal and submitted it to his Qualifying Examination Committee on August 9. (Ex. 5.) Later in the month, when Mr. Susienka was converting his written proposal into an oral presentation for his qualifying exam, he noticed a similarity between the morphological images given to him by Dr. Medici and images from a 2010 *Nature Medicine* article by Dr. Medici on cells that, according to the article, had been treated with other EndMT transitioning agents (BMP4 and transforming growth factor β2, or TGFβ2). According to Mr. Susienka, when he compared them portions of "two of the cell morphology pictures... lined up perfectly." (Ex. 3B, p. 22 [Susienka].)

On August 17, 2013, Mr. Susienka sent Dr. Medici, who was on vacation in London, an email reporting that at least three images in his qualifying exam proposal were the same as images in the 2010 Nature Medicine article. (Ex. 6, p. 1.) Dr. Medici replied on the same day with an email (Ex. 6, p. 2) that, among other statements, advised Mr. Susienka to "calm down," speculated that "this is just a mistake and some of the files got mixed up or they were looking at my old files thinking they were different ones," instructed Mr. Susienka "[d]on't tell anyone about this," and suggested that they meet as soon as Dr. Medici returned. On August 21, Dr. Medici met with Mr. Susienka and told him a postdoctoral fellow who had worked with Dr. Medici at Harvard (Oleg Tsinkalovsky, Ph.D.), and who had done prior work on the project that was now being assigned to Mr. Susienka, must have made a mistake when he transferred computer files to Dr. Medici. (Ex. 3A, pp. 50-51 [Medici].) Over the course of the day, according to Mr. Susienka, Dr. Medici claimed to be waiting for Dr. Tsinkalovsky (by then living in Norway) to send him correct images. (Ex. 3B, p. 30 [Susienka].) According to Dr. Medici, the correct files were already on his computer from an unspecified time in the past when Dr. Tsinkalovsky had placed them there and Dr. Medici was merely trying to locate them. (Ex. 3A, pp. 50-53 [Medici].) In any event, late on the night of August 21, Dr. Medici emailed Mr. Susienka new images to substitute into his qualifying exam presentation the next day $(Ex. 7.)^2$ Mr. Susienka was troubled by the fact that the only images to be replaced were the three he had happened to match to the Nature Medicine article. He did not fully accept Dr. Medici's explanation and became suspicious about the reproducibility of Dr. Medici's EndMT methods. (Ex. 3B, pp. 29, 31, 38 [Susienka].) As he explained in his interview:

Inserting the new images, Mr. Susienka submitted a revised version of his qualifying exam research proposal on August 22. ($\underline{\text{Ex}}$, 8.)

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I mean, it didn't really jive with me completely. I mean, I give people the benefit of the doubt, I think. I make mistakes. I'm not perfect. I'm sure – I guess that with the context of all the issues – like if this had happened out of the blue, I wouldn't have thought a second. I would have thought this is an honest – it is an error.

The fact that we've been trying to do this for like a year at this point and nothing is working, you start to – the wheels start spinning. (Id. at 34.)

In February 2014, Mr. Susienka undertook a closer review of some of Dr. Medici's journal publications and unpublished manuscripts. This was prompted in part by the widely publicized falsification of pluripotent stem cell research findings at the Riken Center for Developmental Biology in Japan. (Id. at 40.) The reported role of manipulated images in that case renewed Mr. Susienka's concerns over the images Dr. Medici had given him for his qualifying exam. (Id.) Over the course of the next several weeks, Mr. Susienka found a number of additional instances in Dr. Medici's work in which micrographs and immunoblotting images appeared to have been used, partially or in their entirety, in more than one manuscript or more than once in the same manuscript and were labeled differently across the manuscripts (i.e., labeled as depicting different experiments and/or results). In addition, he discovered that a fourth image from his qualifying exam presentation, a Western blot of \(\text{B-actin}\), appeared to have been used in a different context in one of Dr. Medici's earlier publications. (Ex. 9, p.1.)

On March 11, 2014, Mr. Susienka met with Elizabeth O. Harrington, Ph.D., the Associate Dean for Graduate and Postdoctoral Education in the Division of Biology and Medicine at the Warren Alpert Medical School, and presented her with his concerns about research misconduct in connection with what he had found. (Id.) In consultation with the Vice President for Research at Brown University, Associate Dean Harrington determined that Mr. Susienka's concerns should be referred to Lifespan/Rhode Island Hospital, which employs Dr. Medici and where Dr. Medici maintains his lab. (Ex. 10, p.1.)

IV. PROCEDURAL HISTORY

On March 31, 2014, Mr. Susienka, accompanied by Dean Harrington, met with Peter J. Snyder, Ph.D., the Senior Vice President and Chief Research Officer for Lifespan. Dr. Snyder functions as the Research Integrity Officer for the Lifespan system. Mr. Susienka presented his allegations concerning the duplicated images he had found in Dr. Medici's manuscripts and publications. A few days later, he raised an additional concern, based on events then underway in Dr. Medici's lab; specifically, he alleged that Dr. Medici was manipulating cell cultures in an EndMT experiment in order to falsely portray the outcome as successful. (Ex. 11, p. 2; Ex. 12, p. 1.)

Mr. Susienka's allegations of research misconduct were determined to be sufficiently credible and specific under the Lifespan Policy on Research Misconduct (Ex. 1) and under 42

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C.F.R. § 93.307(d) to warrant submission to the inquiry process.³ Dr. Snyder appointed a fourmember committee⁴ to conduct the inquiry. The Inquiry Committee was convened and charged on April 8, 2014 The following day, Dr. Snyder sequestered relevant materials from Dr. Medici's laboratory, terminated Dr. Medici's access to the lab, and suspended him with pay. The Inquiry Committee interviewed Dr. Medici and various other individuals with personal knowledge pertinent to the allegations, and on April 28, 2014 issued a draft report concluding there was "strong and credible evidence' for potential Research Misconduct" and recommending "a deeper look into concerns related to on-going research activities in the Medici lab." (Ex. 13, pages numbered P2 and P7.) Following Dr. Medici's submission of comments on the draft report (Ex. 14), the Inquiry Committee finalized its report without revision. On May 20, 2015, Lifespan's Deciding Official, John Murphy, M.D., Executive Vice President for Physician Affairs, accepted the Inquiry Committee's recommendations and asked for the initiation of an investigation into the allegations arising from the information brought forward by Mr. Susienka. This decision was reported to the Office of Research Integrity (ORI) in the U.S. Department of Health and Human Services on May 22, 2014. (Ex. 15.)

Dr. Snyder proceeded to appoint an Investigation Committee.⁵ The Investigation Committee was first convened and charged on June 25, 2014. At the time that this case reached the Investigation Committee, it had been refined and developed through the inquiry process to encompass eight allegations. (Ex. 16.) Four of them concerned allegedly duplicated or repurposed images in journal publications covering work Dr. Medici performed while affiliated with Harvard University (the "Harvard Allegations").⁶ Three of them concerned alleged image duplications or falsification in unpublished manuscripts prepared and submitted to journals

In conducting a preliminary assessment of the allegations pursuant to the federal regulations, Dr. Snyder evaluated the information and images submitted by Mr. Susienka and also provided them in an anonymized format to an independent researcher with expertise in Western blot techniques for an informal assessment of the likelihood of duplication.

The members of the Inquiry Committee were Valerie Knopik, Ph.D., Director of the Division of Behavioral Genetics at Rhode Island Hospital; Michael Carey, Ph.D., Director of the Centers for Behavioral and Preventive Medicine at Miriam Hospital; Alfred Ayala, Ph.D., Professor of Surgery (Research) at Rhode Island Hospital; and Carl Saab, Ph.D., Assistant Professor of Neurosurgery at Rhode Island Hospital (Chair).

The Respondent was notified of the proposed composition of the Investigation Committee and given the opportunity to raise any objections based on unresolved conflicts of interest in accordance with the standards set forth in 42 C.F.R. § 93.310(f). Dr. Chodobski was appointed to accommodate the Respondent's objection to one of the originally proposed members.

Specifically, the following images were alleged to be identical or derived from the same source image:

 [&]quot;Figure S3 C, E-cadherin" and "Figure S4 A, P-Y," both appearing in a manuscript in the April 6, 2011 issue of Matrix Biology;

 [&]quot;Figure ID" and "Figure 2C VE-cadherin," both appearing in a manuscript in the August 1, 2011 issue of Biochemical Journal;

 [&]quot;Figure 5 β-actin" in the August 1, 2011 Biochemical Journal manuscript, and a figure labeled "Smad5" in a manuscript in the February 2, 2012 issue of Osteoarthritis Cartilage; and

^{4) &}quot;Figure_S1.tif β-actin" in an August 10, 2012 PLOS One manuscript, and "Figure 1 FHs74Int 1κB" in a manuscript in the August 11, 2008 issue of The Journal of Cell Biology.

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during Dr. Medici's tenure at Lifespan. The last concerned alleged manipulations of cells in connection with experiments performed at Rhode Island Hospital in April 2014.

Although the Investigation Committee began work on all eight of the allegations and, with respect to the Harvard Allegations, was able based on forensic examination to conclude that the images at issue in the four allegations were in fact duplications, it did not prove necessary for the Committee to make a determination whether the duplications in the Harvard Allegations constituted research misconduct. Instead, following communications with ORI and the Research Integrity Officer for the Harvard Medical School, Lifespan referred the Harvard Allegations to HMS, which accepted responsibility for them on September 18, 2014. (Ex. 17.)

In late September and again in November, Mr. Susienka provided Dr. Snyder and the Investigation Committee with new information concerning additional instances of possible duplication. Observing the same principles for apportioning allegations between the institutions, Lifespan referred the new information to HMS for assessment. At the same time, the Committee took cognizance of the new information for its evidentiary value; as in the case of the original four Harvard Allegations, the Committee examined the additional image duplications alleged in September and November, determined to its satisfaction that the images were in fact duplicates, and left untouched the questions of whether the duplications were purposeful or constituted research misconduct.

Shortly after the September apportionment of allegations between HMS and Lifespan, the Investigation Committee was presented with a revised charge reflecting the reconfigured scope of its responsibilities (<u>Ex.</u> 19), which was also shared with the Respondent. An updated version of the charge, further revised to provide more detail concerning Allegation 2, was provided to the Committee and Respondent on September 29. (<u>Ex.</u> 20.) This report incorporates verbatim the four allegations set out in the September 29 charge and addresses them *seriatim* in Parts VII.A through VII.D.

The Investigation Committee conducted oral interviews and also received documentary and photographic materials from various individuals. In addition to Dr. Medici, who was interviewed on October 7, 2014 (and who provided answers to clarifying written questions on March 23, 2015), the Investigation Committee interviewed the following witnesses: Michael Susienka (September 11, 2014); Diana Ramirez (September 11, 2014); Melissa Ramirez (September 11, 2014); Nedyalka Valkov (September 12, 2014); Olin Liang (September 12,

The table in Exhibit 18, entitled "Summary of Allegations and Implicated Manuscripts/Images," shows for 7 alleged image duplications (coded A through G) all of the publications in which they allegedly appear. (Some of the images were alleged to have been repurposed more than once.) The final column in the table indicates if the associated image (1) pertains to a specific allegation in this case (designated as Allegations 1 and 2); (2) was transferred to Harvard as part of the Harvard Allegations (designated as "REFERRED" with the number associated with the allegation when it comprised one of the original 8, i.e. #1-#4); or (3) was subsequently referred to Harvard for assessment in September or November of 2014 (designated as "REFERRED" with either September or November indicated). Rows 18 and 19 refer to the subject matter of Allegations 3 and 4 in this case rather than to image duplications and were included for the sake of completeness.

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2014); Travis Spangler (January 30, 2015); David Gonzalez (January 30, 2015; by telephone); and Anthony Reginato, M.D. (April 6, 2015).

The Investigation Committee convened in person on the following dates: June 24, 2014; July 16, 2014; July 29, 2014; August 13, 2014; September 9, 2014; September 11, 2014; September 13, 2014; September 17, 2014; September 23, 2014; September 29, 2014; October 6, 2014; October 7, 2014; January 20, 2015; January 30, 2015; and April 6, 2015. The time between meetings was utilized to accomplish additional investigative activities and to review relevant materials and analyses. The Investigation Committee shared with Dr. Medici a Preliminary Report of its findings on May 20, 2015. On July 3, 2015, Dr. Medici submitted to the Investigation Committee a document entitled "Dr. Damian Medici's Response To The Lifespan Investigation Committee's Preliminary Report" (the "Response"). The Response, with all of its exhibits (marked A through PP), accompany this Final Report in the separate binder labeled as Appendix II. The Investigation Committee met once more on July 21 to discuss the Response and related modifications to the Preliminary Report necessary to produce this Final Report.

V. REVIEW OF EVIDENCE

In addition to receiving witness testimony and, in some instances, follow-up written statements, we had available to us various pieces of documentary and photographic evidence, including those portions of the research record available for sequestration at Rhode Island Hospital. The Investigation Committee reviewed and referenced the documentary and photographic evidence taken into custody as necessary and to the extent it was determined to be relevant to the Committee's witness interviews and consideration of the allegations under consideration.

Specifically, as part of its sequestration efforts, the following laboratory notebooks were taken into custody prior to the commencement of the inquiry process or during the course of the inquiry and investigation as their existence or potential relevance became known:

- 1. Melissa Ramirez (Orthopaedics/Regenerative Medicine) (covering 1/2/13 through 7/2/13)
- 2. Melissa Ramirez (Rheumatology) (covering 8/7/13-4/11/14)
- 3. Michael Susienka (covering 1/7/13-4/8/14)
- 4. Diana Ramirez (covering 11/14/12-10/21/13)
- 5. Diana Ramirez (covering 1/2/13-4/3/14)
- 6. David Gonzalez (covering 6/12/13-11/1/13)
- 7. Travis Spangler (covering 1/29/13-7/21/14)
- 8. Cheri Liu (covering 9/24/13-12/13/13)
- 9. Emma Flaherty (covering 2/12/13-6/3/13)
- 10. Agnieszka Blazejczyk (covering 10/11/13-2/24/14)
- 11. Susan Leggett (covering 11/4/13-1/22/14)

As discussed elsewhere in this report, other relevant images and data might have gone uncollected because they remained under Dr. Medici's control and were not made available to us. See Part VI, *infra* ("Preliminary Comments").

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12. Adam Driesman (covering 5/22/13-9/3/13)

Of these laboratory notebooks, the Investigation Committee determined that some did not bear on the allegations under consideration given the content or time-frame of the documented work. The Investigation Committee consulted laboratory notebooks as their potential relevance emerged from the investigation process (through witness interviews, for example).

The desktop computer within the Medici laboratory was also sequestered. A forensically sound clone was commissioned by Lifespan in order to preserve the hard drive and also accommodate the respondent's request to be provided with evidentiary access.

The Investigation Committee was provided with various background documents relevant to the history of the proceedings, including information related to the allegations as raised to and assessed by Dr. Snyder and documents associated with the work of the Inquiry Committee. These documents included various summaries and PowerPoint slides of images, as well as electronic photographs that had been submitted by the complainant to Dr. Snyder and the Inquiry Committee as support for the allegations. The Investigation Committee was also provided with certain photographic evidence by material witnesses in the course of the investigation, and reviewed such evidence in connection with the interviews of the relevant individuals.

As part of its own review, the Investigation Committee collected additional evidence, including the published images in the implicated journals from publically available sources, as well as certain photographic evidence from the computer attached to the microscope in Dr. Medici's laboratory, which is a shared resource of the open laboratory space within which Dr. Medici's laboratory sits. The images collected and preserved on a USB flash drive included all of the images that were contained in a file folder tagged as Dr. Medici's, as well as all of the images taken between Monday, March 24, 2014 and Wednesday, April 9, 2014, the timeframe relevant to work conducted at Rhode Island Hospital and implicated by Allegation 4. Through the collection of these images, the Investigation Committee was able to verify the metadata associated with the photographic evidence referenced above that had been independently submitted by witnesses. The Investigation Committee retrieved copies of certain versions of the unpublished manuscript at issue in Allegations 1 and 2 from the editorial offices of a subset of the journals to which it was submitted, and considered those versions in its evaluation of the related allegations. Miscellaneous other items received or obtained by the Committee in the course of the proceedings include equipment manuals, one witness's iPhone entries, and journal publications relating generally to EndMT research.

Although the Investigation Committee did not review them in the course of its investigation and deliberations, it bears noting that the box of cell samples collected and lysed in

Notwithstanding this determination, all of the enumerated notebooks, in addition to copies of those portions of the laboratory notebooks belonging to Dr. Olin Liang and Ms. Nedyalka Valkov related to work conducted in the Medici laboratory, were made available to Dr. Medici to be responsive to his requests for access. The laboratory notebooks of Dr. Liang and Ms. Valkov were permitted to remain in their possession during these proceedings because Dr. Liang and Ms. Valkov required them for on-going scientific work and because the notebooks were marginally relevant, if at all.

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connection with the experiments at issue in Allegation 4 were removed during the investigation from the laboratory's freezer and sequestered in another location for the purposes of secure preservation.

We have cited and attached as exhibits to this report the pieces of evidence on which the findings outlined in the report are based.

VI. PRELIMINARY COMMENTS

Before taking up the individual allegations in detail, we believe preliminary comments are in order concerning (1) the deliberative independence of the Investigation Committee, (2) the Respondent's access to evidence, and (3) the credibility and candor of the witnesses' testimony.

A. Independence of the Investigation Committee

The Investigation Committee has been mindful throughout these proceedings of our obligation to examine and weigh the evidence objectively. The Response suggests that the results of the investigation were foreordained by Lifespan or driven by prejudgment. (See, for example, Response at pp. 6-7.) We wish to make clear, however, that the conclusions set out in this Final Report reflect the deliberations and decisions of this Committee alone and rest in all instances on our best, considered efforts to discern the truth. We have at no time been under pressure or influence to do otherwise.

B. Respondent's Access to Evidence

The Response repeatedly indicates that Dr. Medici was denied access to evidence that was necessary to his defense against the allegations, implying that the arguments and evidence he has put forward to the Investigation Committee are not as compelling as they might have been absent the "unreasonable restrictions" that he identifies (see Response at p. 6). We are satisfied that Dr. Medici has been given ample opportunity throughout these proceedings to review the evidence in Lifespan's custody related to this matter, and that he had the benefit of the same universe of evidence that was before the Investigation Committee when he commented upon the Preliminary Report and the binder of evidence upon which the Preliminary Report was based. The suggestions in the Response that (1) Dr. Medici did not see potentially exculpatory evidence compiled by Lifespan in this matter, (2) the Investigation Committee considered and based its findings on evidence that was not made available to Dr. Medici, and (3) the Investigation Committee disregarded all potentially exculpatory evidence in reaching its findings, have no merit. As further noted below, the primary limitation on the evidence considered by the Investigation Committee was posed by the relatively sparse amount of evidence supplied by Dr. Medici beyond what the Committee itself was able to identify.

C. Credibility of Witnesses

While our determinations concerning some of the allegations before us turned primarily upon our evaluation of images and documents, all of the allegations to some degree required us to weigh testimonial credibility. Our review of the fourth allegation, in particular, involved

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judgments of the credibility of Dr. Medici on the one hand, and junior members of his lab on the other, including, but not limited to, Michael Susienka, Melissa Ramirez, and Diana Ramirez. We found these members of Dr. Medici's lab to be highly believable. They had positive things to say about Dr. Medici and appeared to harbor no ill will toward him. We perceived no personal agendas on their part and only a fitting regard for the sobriety of this matter. The risk they took as young researchers bringing forth potentially damaging information about an established faculty researcher, their natural reticence to do so, and their offsetting belief that they were morally compelled to act struck us as valiant and sincere. And yet these were only secondary reasons to credit their statements. Our principal reason, we wish to emphasize, lay in our observance of their demeanors, attitudes, testimonial openness, and the cross-consistency of their statements, all of which in combination left us well assured of their probity and honesty.

In contrast, and in the many particulars discussed in our review of the evidentiary record in Parts VII.A through VII.D of this report, Dr. Medici gave us repeated cause to doubt his transparency, forthrightness, and, ultimately, believability. We generally found his demeanor to be defensive, dismissive, or glib. In addition, his testimony tended to be evasive and obfuscating. Finally, he produced starkly little evidence to dispel the allegations against him, and what he did produce was often partial, out of context, or from unexplained sources. Had the evidence truly been what he claimed it to be, we would have expected him readily to present a complete picture – to explain, for example, how image files were organized in his lab or on his laptops, to adduce corroborating information from co-authors on the manuscripts at issue, to address especially troublesome features of the scientific evidence, and so forth. Instead, in a pattern that continued through the submission of the Response, what we received appeared carefully controlled and, at times, intended to divert focus.

In the end, it did not appear to us that Dr. Medici was eager to assist in the fact-finding process. To the contrary, he seemed purposefully to limit what we saw or understood of his exculpatory offerings, and he failed to comply with requests for information or items in his control that we had a reasonable basis to believe might include matter within the scope of the research record. For example:

• The Investigation Committee requested that Dr. Medici produce two laptop computers within his possession, including one that was Lifespan property and one that was believed to have been brought to Rhode Island Hospital from Harvard, so that forensically sound clones could be made and used in connection with the investigation. The Investigation Committee never obtained the requested access. There is little doubt in our minds that relevant information resided there. The Response acknowledges (at page 14) that Dr.

For example, with respect to Allegation 4, we questioned Dr. Medici in his October 2014 interview about steps he had followed in conducting certain experiments in his lab in April 2014. At the time, and when requestioned in March 2015, he recalled little and stated that he could not offer dates and other details without access to his lab and to loose notes allegedly kept there. (See, for example, Ex. 3A, pp. 61, 146, 147 [Medici]; Ex.40, p. 4.) Dr. Medici never availed himself of the opportunity to have supervised access to his lab, and we never located any "loose notes" of the sort Dr. Medici claimed to exist. In his Response, however, he was suddenly able to provide for the first time, and without explaining how, details about what he did and on what day. (Response at p. 4.)

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Medici's "original personal computer" would have provided him "the only ready access he had to any material he might use in these proceedings." ¹¹

- The Investigation Committee made requests for the password to access the Photoshop software that Dr. Medici had installed on his desktop computer in the laboratory. Dr. Medici never provided it and, in fact, has never acknowledged the request.
- The Investigation Committee sought a follow-up videoconference with Dr. Medici to clarify certain aspects of his testimony before the Committee. He conditioned his participation on terms that were unacceptable to the Committee. We later obtained what information we could through written interrogatories.
- Although Dr. Medici implied that his lab contained additional relevant materials and
 repeatedly claimed he was hampered in his ability to defend himself as a result of his lack
 of access to the materials he ignored our requests to specify the materials, where they
 were located, or how they were germane. He did not avail himself of our offer to give
 him supervised access to his lab in order to find such materials.

Despite our ability under federal regulations to draw specific, adverse substantive inferences from and about withheld evidence (see 42 C.F.R. § 93.106(b)(1)), the Investigation Committee declined to do so concerning any of the above. But Dr. Medici's chosen strategy did cause us all the more to question the believability of the selective information he shared with us.¹²

VII. DISCUSSION OF ALLEGATIONS

A. Allegation 1:

Dr. Medici falsified data presented in the unpublished manuscript by Walsh et al. with the draft title, "EndMT Promotes the Natural Regression of Infantile Hemangiomas," which manuscript was submitted to several journals for external peer review and identified as emanating from Rhode Island Hospital ("Walsh Manuscript"), by claiming that the image in the Walsh Manuscript labeled as "Fig. 3c TGF-β2" represented data generated for the Walsh Manuscript when, in

Dr. Medici's Response also claims at page 14 that he offered to "provide a forensic copy" of his personal computer to the Committee. We are aware of no such offer.

We are mindful of the fact that Dr. Medici was represented by outside counsel throughout the investigation, with the result that many of his decisions and positions as a respondent may have been on their advice, it is a respondent's right to secure legal assistance in a misconduct proceeding, and we have done our utmost to understand Dr. Medici's objections and intransigence in that context. That said, represented or not, respondents have every reason to come forward with explanatory or exculpatory evidence if they know it to exist, and one would expect a respondent in possession, or aware, of favorable evidence to be more than willing to guide the fact-finder to it. Dr. Medici's disinclination to cooperate with the Investigation Committee's requests was considered by us in so far as it discredited his suggestions that there was more exculpatory evidence to be had and his claims as to the exculpatory worth of certain submitted evidence.

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fact, the image presented was derived from previously published images labeled as "Fig. 1D p38" and "Fig. 2C VE-cadherin" appearing in the manuscript titled, "Transforming growth factor-B2 promotes Snail-mediated endothelial-mesenchymal transition through convergence of Smad-dependent and Smad-independent signaling," and published in Biochemical Journal on August 1, 2011 ("Biochem J. Manuscript").

1. Factual Background

On March 20, 2013, Dr. Medici submitted to the journal *Nature Medicine* a manuscript (referred to here as the "Walsh Manuscript") entitled "Endothelial-mesenchymal transition promotes the natural regression of infantile hemangiomas." (Ex. 21.) The listed authors were Logan A. Walsh, Diana Ramirez, Melissa Ramirez, John B. Mulliken, and Dr. Medici. The manuscript was rejected on April 17, 2013, and then re-submitted with modifications on July 3, 2013. (Ex. 22.) Dr. Medici uploaded the images that were used in the manuscript. (Ex. 3A, pp. 105, 113 [Medici].) Both the March and July versions contained in Figure 3c an immunoblotting image purporting to show a difference in TGF-ß2 expression levels between hemangioma endothelial cells and regressing hemangiomas. (Ex. 21, Fig 3c [appearing on page 21 and corresponding to the "Figure Legend" for Figure 3 on page 17 of text]; Ex. 22, Fig. 3c [appearing on page 21 and corresponding to the "Figure Legend" for Figure Legend" for Figure 3 on page 17 of text].) Dr. Medici withdrew the manuscript from further consideration by *Nature Medicine* on or around September 30, 2013. The manuscript was then submitted to *Science* on October 18, 2013, with the same Western blot image in Figure 3c. (Ex. 23, p. 15.) *Science* rejected the manuscript in November 2013.

Based on the review he undertook in reaction to the events surrounding his qualifying exams (see discussion in Part III, "General Factual Background," *supra*), Mr. Susienka alleged that Dr. Medici had previously used the image in Figure 3c in an article published in the August 1, 2011 issue of *Biochemical Journal* entitled "Transforming growth factor-ß2 promotes Snail-mediated endothelial-mesenchymal transition through convergence of Smad-dependent and Smad-independent signaling." Mr. Susienka contended that portions of two figures in the *Biochemical Journal* article – Figures 1D (blots of p38) and 2C (blots of VE-cadherin) – not only matched each other but also had been subsequently re-purposed for use in Figure 3c of the Walsh Manuscript. (Ex. 3B, pp. 55-56 [Susienka]; Ex. 24, p. 15.)¹⁵

The Walsh manuscript went on to be submitted to, and rejected by, at least two other journals – *Cancer Cell* and *Cell Stem Cell*. The Investigation Committee was unable to obtain copies of Figure 3c as submitted in those rounds, but Dr. Medici indicated that to the best of his knowledge a corrected version of the figure has never been submitted to a journal. (Ex. 3A, p. 123 [Medici].)

The various dates given above for manuscript submissions and other actions were supplied by editors of *Nature Medicine* and *Science*. See, e.g., <u>Ex.</u> 35.

Findings that are the subject of the Walsh Manuscript, including the immunoblotting image in Figure 3c, may also have been submitted to NIH on February 15, 2013 as part of an electronic Streamlined Non-competing Award Process (eSNAP) progress report for the 4/1/13 = 3/31/14 budget year for Dr. Medici's R01 grant. Because

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2. Respondent's Position

In his prepared statement to the Investigation Committee, Dr. Medici characterized the use of the image that appeared as Figure 3c in the Walsh Manuscript as an "inadvertent error." (Ex. 25, p. 3; Ex. 3A, p. 140 [Medici].) He stated in his interview that he had brought with him "the correct image for Figure [3c], which shows the exact same result as the incorrect image, and I believe that this mix-up is just honest error." (Id.) Before the Inquiry Committee, Dr. Medici also took the position that, in any event, the original image in Figure 3c did not duplicate the images that had appeared in the *Biochemical Journal* article. He stated, "There are several distinct differences between these images [i.e., Figure 3c in the Walsh Manuscript and the images in the *Biochemical Journal* article] which makes clear to me that they are not the same." (Ex.14, p. 6.) He appeared to maintain this position before the Investigation Committee as well. See, e.g., Ex. 3A, pp. 117-20 [Medici].

3. <u>Discussion and Findings</u>

Although acknowledging that Figure 3c in the Walsh Manuscript was incorrect, Dr. Medici had no explanation for how the error occurred or who committed it. During his interview, he showed us on his counsel's laptop computer what he said was the 2011 image that should have been used and walked the computer around for our viewing. We did not see the metadata for the image until the submission of his Response (where screenshots of it appear on the first and last pages of Exhibit D). At that point, we were able to see that the image bore the file name "TGFB2 HemECvsHemMP.jpg," which very precisely reflected what Figure 3C was supposed to depict, namely, a comparison of the expression of TGF-62 by hemangioma macrophages (HemMPs) and hemangioma endothelial cells (HemECs), respectively. In his interview, Dr. Medici also submitted a paper copy of what Figure 3, including Figures 3c and 3e (the subject of Allegation 2, discussed *infra*), would look like had the correct images been utilized. He could not explain the chain of events that led to the incorrect image for Figure 3c having been used in the first place (Ex. 3A, p. 122 [Medici]). Nor did he illuminate how he found the correct image or how he could have chosen to upload an incorrect (and presumably very differently labeled) image file when his file-naming system incorporated specific details about cell types and comparison proteins. 16, 17

of the poor quality of the photo reproductions available to us, we are unable to determine or dismiss this as a fact, but the eSNAP report appears to be reporting the research and findings that are the subject of the Walsh Manuscript.

In his May 2014 written submission to the Inquiry Committee – six months after he had found and submitted the correct images for the Walsh Manuscript to *Nature Medicine* and long before he finally shared the metadata for the image files with us – Dr. Medici wrote that the use of the wrong file folder had most likely been a mistake. He explained, "Our files were often labeled by letter and number codes, so it was easy to get confused." Ex. 14, p. 5. As now appears, however, the file names for at least these files were not random or ambiguous alphanumeric codes, but rather multivariable descriptors whose relevance to the Walsh Manuscript would have been discernible to Dr. Medici and others involved with the reported research.

Through its counsel, the Investigation Committee made requests on four occasions – November 12, 2014 (Ex. 26), December 2 and 4, 2014 (Exs. 27 and 28), and January 9, 2015 (Ex. 29) – for access to the computers in Dr. Medici's possession, but Dr. Medici acceded to none of these requests.

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We note the similarities between Dr. Medici's response in this instance and his responses to (1) Allegation 2 (discussed *infra*), (2) Mr. Susienka's discoveries about the qualifying exam images, and (3) a couple of the alleged image duplications that became part of the Harvard Allegations (see Ex. 14, p. 4 (response to image duplications in *Matrix Biology* and *Biochemical Journal*)). In each instance, faced with an alleged duplication, Dr. Medici claimed simple mistake, attributed the error to identified or unidentified others (see Ex. 3A, pp. 50-51 [Medici]; Ex. 32, p. 2 of attached letter), and produced purportedly correct images from sources never fully shared with his audience. The coincidence of recurring "honest errors" is not impossible, but the veiled corrections spawn questions of their own. With respect to the current allegation, if as Dr. Medici claims the Walsh Manuscript blots did not come from the *Biochemical Journal* images and yet are still incorrect, we are left to wonder what in fact those images reflect and their provenance. Moreover, we are left with the same unease recounted by Mr. Susienka when Dr. Medici replaced only the images in his qualifying exam that Mr. Susienka had specifically called out. Dr. Medici's targeted corrections, reacting only to identified concerns, provoke inevitable but unanswerable questions about other images in the Walsh Manuscript.

We have closely examined the Western blot images labeled TGF-B2 in Figure 3c of the Walsh Manuscript¹⁹ and have found that they are the same as images published in the *Biochemical Journal* article as Figures 1D (labeled as "p38") and 2C (labeled as "VE-cadherin"). More specifically, the Figure 3c bands for HemMP I-58, I-59, and I-60 are identical to the three left-most p38 bands and to the middle three VE-cadherin bands. (See Ex. 30, pp. 15-17.) Besides having been cropped to remove the rightmost p38 and VE-cadherin band, the image in Figure 3c appeared on forensic analysis to have been manipulated to alter the placement and appearance of distinctive artifact appearing above the HemMP I-60 band. These alterations suggest that the duplication of the image was not accidental.

Taken in combination with the several other instances we have noted of Dr. Medici appearing to re-purpose past data to serve in current, unrelated products and with the

We do not know if Dr. Medici has produced correcting images for the *Matrix Biology* and *Biochemical Journal* allegations transferred to HMS; before the Lifespan Inquiry Committee, however, he requested "an opportunity to work with my co-authors to find where the mistakes occurred and to determine whether the incorrect images can be replaced by the correct images for publication as notes of correction." (Ex. 32, p. 2.)

In examining alleged image duplications (whether in connection with this allegation, Allegation 2, or the allegations ultimately referred to HMS), the Investigation Committee started at all times with PDFs downloaded from either *PubMed* or the journal publication itself. In the case of immunoblotting images, where the downloaded image in its unaltered form did not plainly match its alleged twin, a member of the Committee then tested via PhotoShop whether the bands and surrounding artifact of one image or the other had been manipulated by adjusting contrasts, aspect ratios, or other variables. In substance, the Committee retraced and verified the work that Mr. Susienka had already done in his attempts to identify re-used images and to make some of the comparisons contained in his interview presentation (Ex. 24). The Committee, it should be understood, reached its conclusious about alleged duplications independently of Mr. Susienka's analysis. Images and image comparisons from Mr. Susienka that the Committee was not able to verify through its own forensic efforts were not relied upon.

It necessarily follows that we also believe the p38 blots and VE-cadherin blots in Figures 1D and 2C to be the same. Whether that duplication was the result of, or constitutes, research misconduct is not before this Committee. Although such an allegation was before the Inquiry Committee, it was among the Harvard Allegations transferred to HMS to be handled in accordance with that institution's processes.

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observations and fortifying findings discussed with respect to Allegation 2 below, we are persuaded by the preponderance of the evidence that the presentation of falsified data in Figure 3c was intentional and knowing. These actions departed significantly from accepted practices of the Lifespan research community.

B. Allegation 2:

Dr. Medici falsified data presented in the unpublished Walsh Manuscript by claiming that certain images in the Walsh Manuscript labeled as "Fig. 3e" represented data generated for the Walsh Manuscript when, in fact, the images presented were derived from previously published images appearing as Figure 2c in the manuscript titled, "Conversion of vascular endothelial cells into multipotent stem-like cells," and published in Nature Medicine in December 2010. Specifically, it is alleged that the bottom right panel and the top right panel of the image labeled "Fig. 3e" in the Walsh Manuscript are reproduced from images that correspond to the HUVEC/Vector (DIC) and HCMEC/Vector (DIC) panels respectively in Figure 2C of the 2010 Nature Medicine paper.

1. Factual Background

The Walsh Manuscript, as submitted to *Nature Medicine* in 2013, included in Figure 3e eight micrographs depicting cell morphologies. (Ex. 21, Fig 3e [appearing on page 21 and corresponding to the "Figure Legend" for Figure 3 on page 17 of text]; Ex. 22, Fig. 3e [appearing on page 21 and corresponding to the "Figure Legend" for Figure 3 on page 17 of text].) The text described the cells as hemangioma endothelial cells that had been exposed to either a control medium, a hemangioma macrophage-conditioned medium, or a hemangioma macrophage-conditioned medium mixed with antibodies to TGF-β2. (Ex. 21, pp. 5 and 17; Ex. 22, pp. 5 and 17.)

As a result of his February 2014 review of Dr. Medici's publications, Mr. Susienka alleged that two of the micrographs in Figure 3e – one in the panel labeled as HemEC4 cells in "Control Medium + IgG" and the other in a panel labeled as HemEC4 cells in "HemMP Medium + TGF-β2 Ab" – had also appeared in a November 21, 2010 article published in *Nature Medicine*. The article, entitled "Conversion of vascular endothelial cells into multipotent stemlike cells," was authored by Dr. Medici, Eileen M. Shore, Vitali Y. Lounev, Frederick S. Kaplan, Raghu Kalluri, and Bjorn R. Olsen. (Ex. 31.) The two micrographs at issue appeared among six panels in Figure 2c of that article, where the depicted cells were described in one case as human umbilical vein endothelial cells with vector (HUVEC/Vector) and in the other as human cutaneous microvascular endothelial cells with vector (HCMEC/Vector). (Id. at 13.)

According to Mr. Susienka, the HUVEC/Vector image had also been among the several incorrect images that Dr. Medici had given him for his qualifying exam presentation. Mr. Susienka stated that Dr. Medici described the pictured endothelial cells as "HCMECs," not

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HUVECs, and the text of the final as-submitted qualifying exam identified them specifically as human *cerebral* microvascular endothelial cells. (See Ex. 24, p. 3, and Ex. 5, p. 6.)²¹

2. Respondent's Position

Dr. Medici acknowledged that the morphology images used in the original Walsh manuscript were incorrect. (Ex. 14, p. 5.) In a letter transmitted as an email attachment on April 25 to the Inquiry Committee (Ex. 32, p. 2 of attached letter), he characterized the use of the incorrect images as accidental:

I contend that I would not be stupid enough to commit career suicide by intentionally trying to recycle old data and pass it off as something else It is more likely that these observed errors are mistakes caused by accidentally looking at wrong files and thinking they were correct

Dr. Medici stated that he himself discovered the error in the fall of 2013 after the incident in which he furnished Mr. Susienka with erroneous images for Mr. Susienka's qualifying exams. Dr. Medici had attributed the errors concerning the qualifying exam images to a post-doctoral fellow who had worked with him at Harvard. Oleg Tsinkalovsky, Ph.D., and he claimed to have undertaken a review of other materials "that could have been sent to me by the same fellow." (Ex. 14, p. 5; see also Ex. 3A, pp. 97-98 [Medici].) Dr. Medici stated that he discovered all eight of the images in Figure 3e in the Walsh manuscript to be incorrect and that he replaced all of them with correct images before submitting the paper to Science in October 2013. (Id.) In his interview with the Investigation Committee, Dr. Medici circulated briefly and, holding a laptop computer since identified as having been provided by his legal counsel, showed the Committee the eight correct images. (He claims at page 22 in his Response also to have shown the Committee "the meta data and file names" for the images, but this matches the recollection of neither the Committee members nor any of the several staff present at the interview. ²²) In any event, Dr. Medici ultimately included screenshots of the metadata and file names for the correct cell morphology images in Exhibit D to his Response, which he characterizes as "the best evidence in this case." According to the metadata depicted in the screenshots, the eight morphological images were last modified in September 2011 and were labeled as follows:

HemEC2_CM+IgG.jpeg HemEC2_CM+TGFB2Ab.jpeg HemEC2_HMPM+IgG.jpeg HemEC2_HMPM+TGFB2Ab.jpeg

As in the case of the immunoblotting images discussed under Allegation 1, the work that was the subject of the Walsh Manuscript was also reported to NIH on February 15, 2013 as part of the eSNAP progress report for the 4/1/13 - 3/31/14 budget year of Dr. Medici's R01 grant. Figure 2a in the eSNAP report appears to be the same as Figure 3e from the Walsh Manuscript, but we are unable to say so definitively due to the poor reproduction quality of the report.

The portion of Dr. Medici's interview in which the image files were shown corresponds to page 121 and possibly page 122 of his interview transcript. (Ex. 3A.)

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> HemEC4_CM+IgG.jpeg HemEC4_CM+TGFB2Ab.jpeg HemEC4_HMPM+IgG.jpeg HemEC4_HMPM+TGFB2Ab.jpeg

Dr. Medici takes the position that the correct images identified above "show exactly the same results as the incorrect figures" (Response at p. 22) and contends as a result that no falsification occurred and that he would have had no reason intentionally to use the incorrect images.

3. Discussion and Findings

While acknowledging that the original images in Figure 3e of the Walsh Manuscript were erroneous, Dr. Medici had no explanation for how the images came to appear there. (Ex. 3A, p. 100 [Medici].) He did not recall who had provided the original images, and he offered no detail about how or where he had found the replacement images a year earlier (October 2013) when he submitted the corrected manuscript to *Science*. He conjectured that the mistakes were of a sort that happen all the time and suggested that his former associate at Harvard, Dr. Tsinkalovsky, may have been responsible for furnishing him with the wrong images. (Id. at 98-99; see also Ex. 14, p.5.) The Committee did not find Dr. Medici's testimony in these regards credible.

The Committee was troubled by various aspects of Dr. Medici's portrayal of events. We question how or why Dr. Tsinkalovsky, who did not appear as an author on the 2010 *Nature Medicine* article, would have been the keeper and source of its images. We note that the only individual in common between the authors listed on the Walsh Manuscript and the authors of the 2010 article was Dr. Medici, who acknowledged that he had uploaded the images for the Walsh Manuscript. (Id. at 105, 113.) It struck us that Dr. Medici's method of naming morphological files to identify the exact type of endothelial cell used and the differentiating treatment conditions – for example, "HemEC4_HMPM+TGFB2Ab" to signify hemangioma endothelial cells cultured in a hemangioma macrophage medium containing an antibody to TGFβ2 – would have made it hard inadvertently to upload incorrect images (in that particular example, the *Nature Medicine* micrograph depicting a HUVEC cell in vector).

We are troubled as well by Dr. Medici's apparent failure to apprise the co-authors of the Walsh Manuscript of his discovery and correction of incorrect images. Indeed, the history of the Walsh Manuscript presents several curious features. Mr. Susienka first alerted Dr. Medici to the duplicated images in his qualifying exam preparation on August 16, 2013. In his interview Dr. Medici stated, without saying exactly when, that the incorrect micrograph in Mr. Susienka's qualifying exam "prompted me to go back and check micrographs in [the Walsh Manuscript]," which led to his discovery that all of the micrographs in Figure 3e were incorrect. (Id. at 98.) Dr. Medici relied on a similar explanation before the Inquiry Committee, although there he represented that, prior to correcting the image for submission to a journal in October 2013 (now

Asked if he had disclosed the Figure 3e error to his co-authors, Dr. Medici responded, "I honestly don't recall. I mean, as long as it was corrected, I didn't really see anything wrong with it." (Ex. 3A, p. 110 [Medici].)

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understood to be the *Science* submission), the erroneous image resided only on his computer hard drive. (Ex. 14, p. 5.) In August, the Walsh Manuscript had already undergone much of the editorial review process at *Nature Medicine*. At the end of September, however, the manuscript was withdrawn from *Nature Medicine* and, in mid-October, was submitted to *Science* with corrected micrographs substituted into Figure 3e. Dr. Medici appears to have been the moving force behind the decision to withdraw the manuscript from *Nature Medicine*. In a September 26, 2013 email to co-author John Mulliken, M.D., that elicited Dr. Mulliken's consent to the withdrawal, Dr. Medici explained that *Nature Medicine* was taking "an extremely long time":

We have been waiting over 4 months for [external peer review], but still no reviews. The editor requested additional information in the form of an 18 question checklist, which needs to be filled out and sent back to him and will now delay things further.

(Ex. 33.) Before the Investigation Committee, however, Dr. Medici denied that the Nature Medicine checklist played a role in the decision, leading us to wonder if he was merely using the checklist as an excuse with Dr. Mulliken. 24 At the same time, Dr. Medici's communications with Nature Medicine suggest that he was using the checklist, in a slightly different fashion, as an excuse to delay the forward progress of the manuscript and ultimately withdraw it from that publication without ever having to acknowledge the incorrect images. According to an editor at Nature Medicine, Dr. Medici was given the checklist on August 15, 2013. In emails dated August 27 and August 28, he proposed to one of his co-authors making an effort to complete the checklist in short order. (Ex. 34.) According to Nature Medicine's records as described by the journal's editor, however, on September 20 Dr. Medici contacted Nature Medicine and stated that the checklist had been delayed by other demands on his time. (Ex. 35, p. 1.) Finally, on September 27, the day after he told Dr. Mulliken that Nature Medicine was taking too long to send the manuscript out to external review, he emailed Nature Medicine and reported that the checklist would require a meeting with a biostatistician that could not be arranged for another month and that he preferred to withdraw the manuscript. (Id.) It is difficult to square these chains of communication with Dr. Medici's resolute statement to us that the Nature Medicine checklist was "not at all" a factor in the withdrawal of the Walsh Manuscript. (See Ex. 3A, p. 109 [Medici].) With the contrary expressions of his motives we have to wonder if the operative explanation is his concern that the image duplication never come to light with his co-authors or Nature Medicine.

In any event, it is clear to us that the same images appeared in the Walsh Manuscript and the 2010 *Nature Medicine* article (and, for that matter, in one of the micrographs Dr. Medici originally provided to Mr. Susienka for the latter's qualifying exams). We do not believe these recurrences to have been accidental or inadvertent. One of the HemEC panels at issue in the Walsh Manuscript was previously represented as a panel of HUVECs (2010 *Nature Medicine*) and, alternatively, HCMECs (Susienka qualifying exam), while the second HemEC panel at

[[]Dr. Medici]: It was some sort of a new thing they [i.e., Nature Medicine] were doing, working with

some sort of checklist.

Dr. Kurtis; Right.... That was not a barrier in your mind?

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issue in the Walsh Manuscript was previously represented as HCMECs (2010 Nature Medicine). Revisiting Allegation 1, we note that the duplicated immunoblotting images in that instance derived from experiments also dealing with different cell types (HemECs and HCMECs) and there, too, involved authorship lists with only Dr. Medici in common. The suggestion that images for multiple unrelated manuscripts involving different cell types could twice have been derived from a single set of source images by accident requires either remarkable coincidence or an unacceptably disorganized approach to research publication. The proposition asks too much. however, when combined with the fact that the derivative images were not simple duplicates. Rather, the micrographs from the Walsh Manuscript and their counterparts in the Nature Medicine article showed different but overlapping views or regions of the same source images and would have had to have been created by returning to the source images and cropping them down. In view of this purposeful re-engagement with the source material, the extensive pattern of inter-publication duplications that we observed in connection with the Harvard Allegations (as well as the follow-on allegations in September and November), and our overall assessment of Dr. Medici's credibility, we conclude that Dr. Medici knowingly and intentionally falsified the data presented in Figure 3e of the Walsh Manuscript. In doing so, he departed significantly from the accepted practices of the Lifespan research community and engaged in research misconduct.

We reject Dr. Medici's suggestion that the use of incorrect images that "show exactly the same results" as the correct ones falls outside the scope of falsification. Dr. Medici invoked this rationalization repeatedly in his statements and filings. (See, for example, Exhibit 3A, pp. 52-53, 102 [Medici].) It is a flawed suggestion and, if offered ingenuously, disturbing. The representation of images from one experiment as the authentic results of a completely different experiment is falsification regardless of serendipitous similarities. To suggest otherwise upends scientific integrity.

C. Allegation 3:

Dr. Medici falsified and/or fabricated data, specifically an immunohistochemistry image attributed to work performed on equipment at Rhode Island Hospital, presented in the unpublished manuscript by Jorna et al. with the draft title, "ERK5 Regulates Proliferation and Survival of Hemangioma Endothelial Cells" ("Jorna Manuscript"). Specifically, it is alleged that Figure 1A, Hem79, was inappropriately modified to enhance the results.

1. Factual Background

In or around the end of 2012 and early 2013, Lysanne Jorna, a visiting student from the Netherlands conducted certain experiments as a member of Dr. Medici's laboratory using frozen hemangioma specimen samples. The results of these experiments were included in a manuscript (referred to here as the "Jorna Manuscript") entitled "ERK5 Regulates Proliferation and Survival of Hemangioma Endothelial Cells." (Ex. 36.) The listed authors were Lysanne Jorna, Diana Ramirez, Melissa R. Ramirez, Michael J. Susienka, Olin D. Liang, Martin C. Harmsen, John B. Mulliken, Guido Krenning, and Dr. Medici. The Investigation Committee is aware of five journals to which the manuscript was submitted from January 12, 2014 to March 28, 2014. To

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the Investigation Committee's knowledge, the manuscript has not been accepted for publication. (Ex. 3D, p. 60 [D. Ramirez].)

Mr. Susienka, one of the named co-authors on the Jorna Manuscript, alleged that Dr. Medici improperly adjusted the brightness and/or contrast of one of the original images from Ms. Jorna's experiments to produce what appeared as the first panel in Figure 1A. The panel was a consolidated image of hemangioma tissue (labeled as Hem79) described as overlaying immunofluorescent images of phosphorylated extracellular signal-regulated kinase 5 (phospho-ERK5) and the endothelial cell adhesion molecule CD31. It appears in the manuscript as evidence of the conclusion that "[s]trong co-expression of phospho-ERK5 and CD31 was observed in all hemangioma specimens." (Ex. 36, p. 3.) This image and the two other panels of Figure 1A depicting co-location of phospho-ERK5 and CD31 in other hemangioma tissue specimens (labeled Hem107 and Hem129 – id.) were central to the paper's thesis.

Mr. Susienka observed that the consolidated image of Hem79 in the manuscript differed from the consolidated image originally produced by Ms. Jorna. Based on the high degree of background fluorescence seen in Ms. Jorna's original red-channel image of phospho-ERK5, Mr. Susienka suspected that the fluorescence in the red channel was due to tissue autofluorescence as opposed to the presence of phospho-ERK5. (Ex. 37, p. 2.) After experimentally adjusting the original images, Mr. Susienka believed that the "strong co-expression" shown in Figure 1A for Hem 79 could have been achieved through adjustments in brightness and contrast rather than strong signaling of phospho-ERK5. It was Mr. Susienka's testimony that Ms. Jorna took the original images on the laboratory microscope, but that Dr. Medici viewed them "side by side" with Ms. Jorna, raising the possibility that the image modifications were made at Dr. Medici's direction. (Ex. 3B, p. 74 [Susienka].)

As an additional reason for questioning the authenticity of the Hem 79 image, Mr. Susienka questioned whether the original immunofluorescence image could have been produced using the secondary antibodies that his records indicated were available in the laboratory at the time of the experiments. (Ex. 37, p.2.) Mr. Susienka's recollection was that Ms. Jorna had used a type of secondary antibody (Alexa Fluor 647 Donkey Anti-Rabbit IgG, Invitrogen catalog #31573) that Mr. Susienka had ordered for the laboratory on October 31, 2012. He questioned whether this type of secondary antibody would have been compatible with the G-1B filter for visualizing red fluorescence on the microscope that he believes Ms. Jorna used. (Id.) Mr. Susienka stated in his allegation that he "did not order the correct secondary antibodies for that filter (Alexa Fluor 568 Donkey Anti-Rabbit IgG, Invitrogen catalog #A10042) until April 25, 2013," after Ms. Jorna's March 2013 departure from the laboratory. In response to questioning by the Investigation Committee, Mr. Susienka could not say definitively whether he

Mr. Susienka testified that he "felt it was [his] fault secondary antibodies were wrong because [he] ordered everything for the lab." (Ex. 3B, p. 75 [Susienka].) We did not take this as a literal statement that he, as opposed to the lab administrator, actually placed all orders. Rather, we understood him in context to say that he chose the secondary antibodies that would be ordered for the fluorescence microscope. We therefore do not find a contradiction between his testimony and Diana Ramirez's testimony about lab purchases being placed by the lab administrator. Dr. Medici suggests in his Response that the contradiction is not only real but also so significant as to render Mr. Susienka a non-credible witness for all purposes. We disagree.

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communicated to Dr. Medici his belief that the wrong secondary antibody had been used in the experiment. (Ex. 3B, pp. 76-77 [Susienka].)²⁶

2. Respondent's Position

In his interview, Dr. Medici stated in regard to Allegation 3 that Ms. Jorna conducted the experiments and provided him with the images. (Ex. 3A, p. 131 [Medici].) He stated that he knew "absolutely nothing about" whether, in conducting the experiments, Ms. Jorna may have used an antibody that would not have been detectable by the microscope on which the immunofluorescent images were captured. (Id.) In his prepared statement to the Investigation Committee, Dr. Medici stated that "enhancements of brightness, contrast, and color balance are customary and permitted according to the standard guidelines for figure preparation in scientific journals." (Ex. 25, p. 1; Ex. 3A, p. 134 [Medici].) He also noted that to the best of his memory he "did not enhance this image," and that "Lysanne Jorna did the immunohistochemistry and provided the images." (Ex. 25, p. 1; Ex. 3A, p. 135 [Medici].)

3. Discussion and Findings

After careful review, we conclude that the preponderance of the evidence before the Investigation Committee with respect to this allegation does not support a finding of research misconduct.

First, the testimony before the Investigation Committee is ambiguous with respect to Dr. Medici's involvement in the creation of the image in question. Dr. Medici testified that Ms. Jorna provided him with the images that were used in the manuscript, whereas Mr. Susienka's testimony suggests that Dr. Medici, while showing Ms. Jorna how to make composite images, might have directed the image adjustment process. Although we believe Ms. Jorna and Dr. Medici worked together while viewing the images, it is a leap to conclude on that basis alone that Dr. Medici performed or controlled the production of the consolidated image in question.

Second, even if the Hem79 panel of Figure 1A in the Jorna Manuscript reflects enhancements of contrast and manipulations of brightness, such adjustments are common and accepted analytical and interpretive aids under prevailing scientific standards. This is not to say that such adjustments cannot cross the line between enhancement and falsification. We are simply not prepared to say on the evidence before us that the image adjustments in this instance did so or departed significantly from accepted practices of the relevant research community.

Finally, the evidence concerning secondary antibodies is not sufficiently probative to sustain the allegation. The possibility that the preferable secondary antibody, Alexa Fluor 568, was used has not been adequately ruled out. The original phospho-ERK5 image produced by

Based on its review of the already available evidence, the Investigation Committee did not feel it was necessary to attempt to contact Ms. Jorna, who departed Rhode Island Hospital over a year before these allegations came to light and appears now to reside in the Netherlands. In deciding whether to pursue additional witnesses, the Investigation Committee was mindful of balancing its information needs against the Respondent's confidentiality interests.

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Ms. Jorna appears to exhibit a strong signal, suggesting that an appropriate secondary antibody was used. The Moreover, even if it could be established that Ms. Jorna used Alexa Fluor 647, that would not prove that her original image fails to reflect phosphorylation of ERK5. According to the G-1B filter manufacturer, the narrow excitation wavelength for the filter centers around 546 nm. (Ex. 38, p. 4.) We note that this lies at the low end of the excitation range of Alexa Fluor 647, creating at least the theoretical possibility of signal emission. (See Ex. 39.) The Investigation Committee does not doubt the sincerity of Mr. Susienka's concerns and recollections detailed in Exhibit 37. However, we do not feel that the questions surrounding the reagents used in Ms. Jorna's work afford an adequate basis to judge the Hem79 image in Figure 1A to be anything other than what it purports to be.

D. Allegation 4:

Dr. Medici falsified and/or fabricated data by manipulating live cell cultures to achieve a desired response while in the course of conducting research at the Rhode Island Hospital. Specifically, it is alleged that Dr. Medici manipulated the results of an experiment to make it appear to have been successful by supplementing endothelial cells undergoing the EndMT experimental process with pre-existing mesenchymal cells.

1. Factual Background

In the spring of 2014, Dr. Medici became frustrated with the difficulty that members of his lab had been experiencing over many months in their attempts to achieve successful EndMT outcomes. (Ex. 3A, pp. 63-64, 135-36 [Medici]; Ex. 3D, p. 19 [D. Ramirez].) He decided to go into the lab and attempt to perform the process himself. In his experiments, carried out in late March and the first week of April (hereafter referred to as the "April Experiments"), he used HDMECs and followed the protocols his students and trainees had been following for their respective projects. (Ex. 3A, pp. 136-137 [Medici].)

Dr. Medici obtained the supply of HDMECs for the April Experiments from Michael Susienka (Ex. 40, p. 3) in or around the last week of March, passaging the cells into flasks that were placed in the laboratory incubator with the label "HDMEC/P=6/3-28." (Ex. 3B, pp. 60, 67 [Susienka].) He also stored flasks of mesenchymal cells in the lab incubator. (Ex. 3A, p. 78 [Medici].) Those flasks bore the label, "HDMEC/EndMT/3-30." According to Dr. Medici, the mesenchymal cells were to be used as positive controls in his experiments and were brought with

Inexplicably, the materials in Dr. Medici's lab available for sequestration did not include a hard copy of Ms. Joma's laboratory notebook. As a Principal Investigator and head of his laboratory, Dr. Medici was responsible for the preservation of source data and notes from the experiments conducted under his supervision. Although Dr. Medici has ventured that Lifespan lost Ms. Jorna's notebook following its sequestration of lab materials and insimuated that Mr. Susienka may have knowledge of what became of the notebook, we credit neither theory. We note that Dr. Medici has offered nothing to suggest that the notebook was retained in the lab in the first place. Given his continuing work on the preparation and multiple submissions of the manuscript, we would expect him to have been able to attest to at least this much.

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him from Harvard where they had been created by a colleague through the EndMT process. ²⁸ (Ex. 3A, pp. 75-77 [Medici].)

Mr. Susienka discovered Dr. Medici's flasks, which according to Mr. Susienka totaled eight in all, in the incubator on April 1. He photographed the two types of flasks (Ex. 30, p. 4) and texted two of his colleagues, Melissa and Diana Ramirez, telling them only to look in the flasks the next day. (Ex. 3B, pp. 69-70 [Susienka].) He made no mention of why he wanted them to look in the flasks. (Id. at 70.) Diana Ramirez had worked in Dr. Medici's lab as a research assistant since late 2012. (Ex. 3A, p. 15 [Medici].) Her sister Melissa had been an intern in the lab (id. at 15-16) but, by the time of the April Experiments, was working in the lab of Dr. Anthony Reginato, who was collaborating with Dr. Medici on EndMT work directed at research into sclerodermal fibrosis.

On April 2, as prompted by Mr. Susienka's text message, Melissa and Diana each on their own visited and examined the incubator. Both were shocked to find flasks of what they identified as pure populations of mesenchymal cells. (Ex. 3C, p. 23 [M. Ramirez], as amended, Ex. 3D, p. 21 [D. Ramirez].) The discovery provoked their suspicions about Dr. Medici's intentions.²⁹

That same afternoon, Mr. Susienka and Melissa Ramirez observed Dr. Medici plating the contents of his flasks into what they estimated to be about 20 six-well plates. To both it appeared that Dr. Medici had plated materials from all of his flasks, and Ms. Ramirez noted that

Dr. Medici was unable to say who at Harvard had created the mesenchymal cells. (Ex. 40, p. 2.) A competing but unproved explanation for the provenance of the cells can be found in Diana Ramirez's testimony. Diana was in charge of a supply of mesenchymal cells purchased from a national supplier (ATCC) around mid-March. (Ex. 3D, p. 8 [D. Ramirez].) She divided the supply into 20 cryovials that she froze and kept in the laboratory's liquid nitrogen freezer, later giving one vial to one of the undergraduates in the lab. She stated that Dr. Medici came to her in late March, "a couple of days" before he began culturing his HDMECs, to ask her where the mesenchymal cells were stored. (Id. at 8-10, 22, as amended.) On April 3, after seeing that there were new flasks of mesenchymal cells in the lab incubator, Diana checked the cryovials and found that one was missing, leaving her with only 18. (Id. at 10, 21, and 23.) Although we found Diana credible, we do not need to speculate whether the flasks of mesenchymal cells in the incubator on April 1 came from her frozen supply or, as Dr. Medici claimed, from a source at Harvard. The fact that mesenchymal cells were indisputably available in the lab at the time of the April Experiments is the material point.

Various of her observations struck Melissa Ramirez, rightly or wrongly, as irregular. She thought it strange that flasks of mesenchymal cells would be stored in the incubator when the object of Dr. Medici's experiments was to produce mesenchymal cells. (Ex. 3C, p. 23 [M. Ramirez].) In addition, under the microscope, the population of mesenchymal cells appeared too pure – devoid of cell death or untransformed endothelial cells – to be the product of EndMT, as the flasks were labeled. (Id. at 25-26.) Finally, the very fact that flasks carried the label EndMT seemed unusual, since transformations were ordinarily done on plates. (Id. at 26, as amended.) Dr. Medici, however, stated that the flasks were labeled "EndMT" because, as noted earlier, they reflected the product of a mesenchymal transition performed at Harvard and he was in the process of growing out the population, not performing EndMT. (Ex. 40, p.3; Ex. 3A, p. 77 [Medici].) Furthermore, he indicates in the Response that in expanding both types of cell lines (HDMEC and endothelial derived mesenchymal cells) in anticipation of the April Experiments, he kept "the two different cell types separate at all times." (Response at p. 27.)

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none of the original flasks was in the incubator on the following day. (Ex. 3C, p. 23 [M. Ramirez], as amended.) Also on that afternoon, Dr. Medici gave Ms. Ramirez two of his plates of HDMECs to treat with bleomycin, as she was working at that time on an EndMT experiment in which she planned to treat a different type of endothelial cells, HUVECs, using bleomycin as the transforming agent. (Ex. 3C, p. 22 [M. Ramirez]; Ex. 43, p. 109.) Bleomycin is a hazardous compound that Ms. Ramirez had been trained and qualified to work with; as he acknowledged, Dr. Medici was not trained to handle it and never did so. (Ex. 3A, pp. 71-72 [Medici].)

Putting aside for now the plates that awaited treatment with bleomycin, it is unclear when Dr. Medici would have applied transforming agents – TGFβ2, BMP2, or others – to the treatment rows (the bottom three wells) of his 6-well plates of HDMECs. He states in his Response that he did so on April 3; there are no witnesses or documents either to support or contradict the claim.³² In any event, on Friday, April 4, both Mr. Susienka and Melissa Ramirez examined and photographed the cells in Dr. Medici's plates. Mr. Susienka, who looked at two of

Notes from Mr. Susienka include the following entry for April 2, 2014: "Damian spends most of his afternoon working in the tissue culture room to passage the cells from the eight T75 flasks to ~20 6-well plates for his various experiments." (Ex. 11, p. 2.) Melissa Ramirez also created the following note on her iPhone at 4:08 p.m. on the same day: "A few minutes ago and currently, Damian is in the cell culture room splitting what seem to be all his flasks into several plates. My guess would be about 16-20 plates." (Ex. 41.) The evidence from Dr. Medici on these matters is more oblique; he recalled plating his experiments on "either April 1 or April 2," stated that "the flasks were split into plates before April 9," and also noted that "one of the flasks of positive control cells (the transformed HDMECs) mysteriously went missing during that week." (Ex. 40, p. 3.)

Dr. Medici and Melissa Ramirez cast the context and nature of their roles differently. They agree that Ms. Ramirez was a member of Dr. Reginato's lab and was working on rheumatological research involving bleomycininduced EndMT of HUVECs. Dr. Medici claims that he offered Ms. Ramirez surplus HDMECs left over after he created the plates for his experiments and that it was up to her whether she wanted to expand her project - from which he divorces himself - to include two types of cells, HUVECs and HDMECs. He portrays Ms. Ramírez as an independent researcher; he "did communicate with Ms. Ramirez about when her reagent should be added, but he did not direct or oversee her experiment." (Ex. 40, p. 4.) Ms. Ramirez, however, considered Dr. Medici to have more say in what she was doing. She noted that Dr. Reginato and Dr. Medici were collaborating on a protocol "that used an established animal model of skin fibrosis with bleomycin as the treatment." (Ex. 42, p. 1.) The two PIs were collaborators in their research and in their supervision of Ms. Ramírez, a point confirmed by Dr. Reginato in his interview. (Ex. 3G, pp. 8-9 [Reginato]; see also Ex. 3A, p.70 [Medici].) According to Ms. Ramirez, Dr. Medici "did not agree with using this HUVEC cell type for an in vitro skin fibrosis experiment." Dr. Medici "wanted to use HDMECs, and showed me where plates he setup with cells were in the incubator for me to add bleomycin." (Ex. 42, p. 1; Ex. 3C, p. 20 [M. Ramirez].) From her standpoint, Dr. Medici was jointly overseeing her work, a perspective that Dr. Reginato appeared to share. (See Ex. 3G, p. 28 [Reginato]; see also Ex. 41 (M. Ramírez iPhone entry from 4:08p.m. on April 2: "Around 2p.m., Damian asked me if I was around for the next couple of days to treat some homecs with bleomycin.") Although the Investigation Committee was satisfied that Dr. Medici was the driver of the HDMEC bleomycin experiment assigned to Ms. Ramirez and any treatment would have been in response to his request, the point is academic in the end. Research misconduct can occur regardless of whether the perpetrator is an identified collaborator on the experiment that he or she falsified or fabricated.

Dr. Medici did not maintain a lab notebook for the April Experiments. (<u>Ex.</u> 3A, p. 61 [Medici]; <u>Ex.</u> 14, p. 7.) He stated that he kept loose notes of the April Experiments in his lab but neither provided specific directions to them nor took us up on our offer of supervised access to the lab to locate them. (<u>Ex.</u> 29.) On our own we were unable to find any pertinent notes in his lab.

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the plates at 12:30 p.m. (see \underline{Ex} . 44, p. 1; see photos of plates at \underline{Ex} . 45), noted that mesenchymal stem cells were already very much apparent in the treatment wells:

[T]he TGF-B2 (T2) "treated" wells already exhibit perfect mesenchymal stem cell morphology (and no cell death) and the vehicle (V) "[un]treated" wells exhibit perfect endothelial cell morphology (and no cell death). Also, the treated (T2) wells appear to be more confluent than the untreated (V) wells, which makes no sense because the treatments should induce a noticeable amount of cell death (as [Dr. Medici] has told us numerous times before and we have all seen in our attempts to replicate these experiments. (Ex. 44, p. 1; see photos of cells and origin wells at Ex. 24, p. 21.)

Ms. Ramirez's observations from that Friday were to the same effect. She examined and photographed cells from all 24 wells on four of Dr. Medici's plates and "saw that the whole top three wells which is usually where we put our controls . . . were perfectly round and the bottom rows which would be where we would add the growth factors were spindle shaped exactly how the spindle-shaped [i.e., mesenchymal] cells in the flasks . . . looked." (Ex. 3C, pp. 30-31 [M. Ramirez], as amended.) (The 24 photos of the contents of the wells (including one blank) appear in Exhibit 46; we have superimposed labels on each of the 24 photos, indicating the digital file name that Ms. Ramirez assigned to the photos and whether the cells are from vehicle wells or treatment wells.) In addition, she noticed the presence of two small orange-capped flasks placed out of sight behind the stacks of plates, which appeared to have been labeled in Dr. Medici's handwriting. (Ex. 3C, pp. 83-86 [M. Ramirez].)

Two days later, on April 6, Dr. Medici sent Ms. Ramirez an email, entitled "HDMEC EndMT," attaching images (presumably from his experiments) of "HDMECs treated with vehicle or TGFB2." (Ex. 47, p. 1; Ex. 3C, p. 46 [M. Ramirez], as amended.) The images were similar to what Ms. Ramirez and Mr. Susienka had already seen for themselves two days earlier. Dr. Medici, referring to the two plates of HDMECs he had given Ms. Ramirez for bleomycin treatment, also noted, "If your bleomycin treatment works you should see something similar." (Id.)

Over this same period, Ms. Ramirez had continued to observe the two plates of HDMECs given to her for bleomycin treatment. Dr. Medici had wanted her to do the treatment on Thursday, April 3. (Ex. 3C, p. 39 [M. Ramirez].) She did not do so, noting in her lab notebook that neither the plates of HDMECs nor the plates of HUVECs she planned to treat in connection with her research for Dr. Reginato were yet at the target confluency of 80-90%. (Ex. 43, page numbered 109.) On Friday, April 4, Dr. Medici again instructed Ms. Ramirez to proceed with the treatment. Without telling him so, she again refrained. (Ex. 3C, pp. 40-42 [M. Ramirez]; Ex. 42, p. 1.) Her lab notebook contains an entry indicating that the confluency was too low for bleomycin treatment on Friday and that she would check them again on Sunday. (Ex. 43, page

It is not altogether clear what time Ms. Ramirez made these observations. Her lab notebook does, however, indicate that she was in the lab examining the confluency of endothelial cells in other plates at 7 p.m. (Ex. 43, page numbered 111.)

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numbered 111.) In reality, however, Ms. Ramirez had by then independently decided that she was not going to treat the HDMECs, and she communicated this intention to both her sister and Mr. Susienka on that Friday. (Ex. 3C, pp. 41-44, 70-71 [M. Ramirez]; Ex. 3B, pp. 72-73 [Susienka]; Ex. 3D, pp. 40-41 [D. Ramirez].)

Ms. Ramirez was out of the lab on Saturday, April 5, and did not again see the two HDMEC plates until Sunday evening. Dr. Medici told Ms. Ramirez he would check on them over the weekend (Ex. 3C, p. 42 [M. Ramirez]) and, by his account, he came in on Friday or Saturday (Ex. 40, p. 4). At 7 p.m. on Sunday, Ms. Ramirez examined the HDMECs and found dramatic changes in the experimental wells. She described her observations:

I was actually horrified at what I saw. I saw a mixture of round cells and spindle-shaped cells.

There was a transformation. There shouldn't have been – there should not have been more cells than what was treated.

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So I saw more cells where the treated cells should be. Knowing what I know, with the Bleomycin treatment, there should be a lot of cell death. . . . I mean, there shouldn't have been anything that happened to these cells. The fact that just the bottom was covered with round and spindle-shaped cells and on the top there were less cells, all round, should not have happened. (Ex. 3C, pp. 42-43 [M. Ramirez].)

Ms. Ramirez photographed the wells and left. (Exhibit 48 contains a well-by-well comparison of the cells as they appeared in photographs taken on April 4 and April 6, behind a photograph taken by Ms. Ramirez of the physical plates themselves.) On the following day, Monday April 7, Dr. Medici sent her an email with the subject line, "HDMEC Bleomycin EndMT," to which he attached images of endothelial cells (presumably from a vehicle well) and spindle-shaped cells (presumably from an experimental well). (Ex. 49.) On that day or the next, when she was again in the lab with Dr. Medici, he asked her to lyse the cells, but she left the lab and went home, explaining that her mother was ill. (Ex. 3C, pp. 61-63 [M. Ramirez].) Ms. Ramirez never told Dr. Medici that the HDMECs had been left untreated and never had anything more to do with them. On Thursday, April 10, after a day away from the lab, she met with Dr. Snyder, who had been given her name by Mr. Susienka. (Id. at 63-64.)

2. Respondent's Position

In his statements and submissions to the Investigation Committee, Dr. Medici has unequivocally denied manipulating any of the HDMEC cell cultures to achieve falsified results. (See, e.g., <u>Ex.</u> 3A, pp. 137-39 [Medici].) He points out that "[t]he purpose of troubleshooting

Ms. Ramirez recalled Dr. Medici indicating he would stop into the lab on Saturday. (<u>Ex.</u> 3C, p. 45 [M. Ramirez]; <u>Ex.</u> 42, p. 1.)

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was to identify why experiments were failing, so sabotaging my own cultures would be counterproductive and would not resolve the issues we were having." (Id.)

With respect to all of the plates other than the two that were to undergo bleomycin treatment. Dr. Medici's position is that he "treated the cells according to my lab members' conditions." (Ex. 3A, p. 137 [Medici].) He explained what ensued as follows:

It usually takes 24 to 72 hours for the cells to transform. I came into the lab over the weekend to check the cells and it looked like the cells had transformed, as they should have, based on what is already known about inducing EndMT in the scientific literature.

In my opinion, and I have been doing this for many years now, I believed at the time that the cells had transformed, even though I had never previously attempted EndMT on HDMEC cells before. (Id. at 137-38.)

With respect to the two plates of cells that he expected Melissa Ramirez to treat with bleomycin, Dr. Medici noted that he "cannot confirm . . . that Ms. Ramirez actually did not treat her cells." (Ex. 40, p. 6.) He contended that Ms. Ramirez's lab notebook does not reflect her claim. Declining to speculate about what she did, he "can only state that Ms. Ramirez told him she had treated the cells, [and] that a flask of his positive control [mesenchymal] cells went missing prior to Dr. Medici being shown, by Ms. Ramirez, what she reported as the results of her bleomycin treatment." (Id.) In the Response, Dr. Medici reiterates the possibility that Ms. Ramirez did in fact treat the HDMECs with bleomycin resulting in a successful transformation. (Response at p. 29.) The Response suggests two additional theories to explain the dramatic morphological changes; first, that another person (Melissa Ramirez, Diana Ramirez, Mr. Susienka, or an unnamed member of the laboratory) tampered with the experiment (id. at p. 28); and second, that the HDMECs "spontaneously transformed" (id. at p. 29). The latter argument relies on a journal article from January of this year that Dr. Medici brought to our attention in March: Huang, L. et al. (2015), Glucose transporter 1-positive endothelial cells in infantile hemangioma exhibit features of facultative stem cells. Stem Cells 33, 133-145. (Ex. 51.) Notwithstanding our having noted in the Preliminary Report why the experimental conditions reported in the Huang article lend no reasonable support to the notion of "spontaneous transition" in this case. Dr. Medici presses the theory still (see, for example, Response at p. 16).

3. <u>Discussion and Findings</u>

a. Meaning of "Research"

A threshold issue is whether Dr. Medici's April Experiments constituted "research," as the term is used in the Lifespan policy and the PHS regulation. We note that Dr. Medici has made a point of describing the experiments at all times as "troubleshooting" and continues to do so in the Response. The term is not legally significant or even readily defined, but we are left to wonder if his choice of terminology is deliberate and meant to suggest that he was engaged in

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something too casual or routine to be dignified as research. We, however, do not doubt that the April Experiments, however labeled, constituted research.

Dr. Medici's explanations make clear that he was attempting to confirm, refine, or establish protocols that would reliably induce EndMT in HDMECs. He had never worked with HDMECs and had opted to concentrate on them precisely because "we wanted something novel." (Ex. 3A, p. 24 [Medici].) He was not simply correcting known errors of his lab members, because he did not know for a fact that the EndMT problems were traceable to them. In fact, he considered it a possibility that the protocols being followed in his lab would require alteration:

I had become increasingly frustrated with my junior lab members['] inability to or struggle to induce this when it was a well-published mechanism. As I told you, I figured it could have been a few different things. It could have been cell type was different. Maybe they, you know, reacted differently to different stimuli. Maybe they needed a different dose. (Id. at 63, as amended.) 35

Given the essentially exploratory character of his undertaking, whether to confirm the existing protocols for his trainees or to arrive at new ones for their instruction and adoption, we doubt that anyone in our research community would consider the April Experiments to be anything other than research.

More technically, the PHS regulation and Lifespan Policy define research to include "a systematic experiment... designed to develop or contribute to general knowledge (basic research) ... relating broadly to public health by ... confirming information about, or the underlying mechanism relating to, biological causes, functions or effects, diseases, treatments, or related matters to be studied." 42 C.F.R. § 93.222. Nothing in the definition indicates that attempts to replicate a technique or process carried out by other researchers cannot itself constitute research. We believe that the regulations were meant to apply broadly; any suggestion that a "troubleshooting" label would cloak experiments from scrutiny under the regulations is finer hair-splitting than the rules or the Lifespan Policy seem to contemplate.

Finally, the context and reality of the April Experiments must be borne in mind. Dr. Medici's troubleshooting experiments were part and parcel of the larger research endeavors of his lab. Several ongoing research projects in his lab depended on demonstrating the EndMT process. This step had stymied his students and trainees. No less than any other part of a research protocol, the investigation into whether this hurdle was surmountable was research. Indeed, notwithstanding Dr. Medici's representation that his work was never intended for publication, it appears entirely possible that any usable results he obtained would have been made available to others to use. By his account, for example, the HDMECs he plated and gave

See also Ex. 3A, p. 41 [Medici] ("[I]n my opinion, I felt that there could be a number of reasons for that; their technique was bad. Either the protocol needed to be changed. It needed a different dose. It needed more time or that, you know, the cell line was different. So maybe they just expressed different levels of receptors and don't behave the same way in response to certain stimuli than other cell type would.").

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to Melissa Ramirez were given to her for use in the scleroderma research that Dr. Reginato was doing (which, according to Dr. Reginato, Dr. Medici was overseeing). (Ex. 40, p. 4; Ex. 3G, p.28 [Reginato]) Similarly, according to notes from Mr. Susienka, at an April 8 lab meeting in which Dr. Medici announced the successful outcome of his EndMT efforts, Dr. Medici –

tells me that he has cell lysates (for western blotting) and Trizol samples (for PCR) from some of his EndMT experiments that he did for me using some of the compounds I have tried to use to induce EndMT (BMP2 and CDDO-EA, specifically). He says he's "not sure if it worked or not" but that "it looked like the cells transformed" and that I should "quantify the protein in the samples . . ." and then "run some western blots for EndMT markers" before trying PCR on the Trizol samples. (Ex. 44, p. 1; emphasis added.)

In the past, Dr. Medici had stepped in and performed the EndMT step for students in his lab whose own efforts had been unsuccessful, ³⁶ and it appears that he contemplated that at least some of the products of his April Experiments would be seamlessly integrated into the work that others were doing under his supervision. ³⁷ To conclude that, all of this notwithstanding, the April Experiments did not constitute research would flout reality.

b. Alleged Manipulations

Turning, then, to the allegation of falsification through manipulation of the EndMT cultures, we believe it helpful to differentiate between the HDMECs whose treatment Dr. Medici kept under his control (to be treated with TGFβ2, BMP2, and other transforming agents) and the HDMECs he entrusted to Ms. Ramirez for treatment with bleomycin. In both cases, what is alleged is that the experimental wells of HDMECs did not undergo EndMT and that the apparent transitions were achieved instead by Dr. Medici having simply placed in the wells, or added to them, mesenchymal stem cells from another source. The bodies of pertinent evidence, however, differ as between the two experimental subsets.

With respect to the HDMECs that Dr. Medici claimed to have treated himself, the principal evidence consists of Mr. Susienka's and Melissa Ramirez's April 4 observations and photographs of Dr. Medici's culture plates, with the central question being whether we can infer

David Gonzalez, an undergraduate researcher in Dr. Medici's lab from approximately June 2013 to May 2014, testified that he did not achieve EndMT. However, in August 2013 he set up an experiment for which Dr. Medici agreed to perform the EndMT portion while Mr. Gonzalez was on vacation. (Ex. 3H, pp. 12-18 [Gonzalez].) Dr. Medici "actually physically" did "the experiment and collected the samples for" Mr. Gonzalez, who then performed the subsequent biochemical analysis on them. (Id. at 12-13) This particular experiment "worked really well" according to Mr. Gonzalez. (Id. at 12.)

Travis Spangler, who worked as an undergraduate researcher in Dr. Medici's lab and is now a second-year medical student, testified that he received cells from Dr. Medici derived from the April Experiments, which he lysed and on which he was expected to perform biochemical analyses in connection with his on-going experiment exploring the differentiation of mesenchymal cells produced through EndMT to tenocytes (tendon cells). (Ex. 3F, pp. 13, 15-17 [Spangler].)

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manipulation from the morphological state of the cells in the experimental wells and what is known about the EndMT process.

Mr. Susienka felt the April 4 observations made no sense in terms of Dr. Medici's EndMT protocol timeline, explaining:

[I]f he plated the cells into the 6-well plates on 4/2, the cells would have needed to attach overnight, and then he would have had to serum-starve them on 4/3 and then start treating them on 4/4. Furthermore, EndMT should not be obvious morphologically until 48-72 hours later (as he has told us numerous times before), which would . . . have been on 4/6 or 4/7.

(Ex. 44, p. 1.) In his interview, Dr. Medici agreed that serum starvation was part of the protocol to be observed (Ex. 3A, pp. 25-27 [Medici]), but he did not specify a required duration. Moreover, he gave a different transformation range, stating, "For the things I have personally done in the past, the cells would usually transform anywhere between one day and three days, so 24 to 72 hours." (Id. at 27.) Viewing one of the April 4 photos of cells from the experimental wells, Dr. Reginato stated that without knowing the dose or type of transforming agent that had been used he was unable to say how much time the apparent transformation would have taken "[b]ecause it could be 24, could be 72 hours." (Ex. 3G, p. 25 [Reginato].)

On this record, and having nothing to contradict Dr. Medici's claim of having in fact added one or more transforming agents, we are unable to say whether the morphological changes depicted in Mr. Susienka's and Ms. Ramirez's photographs were due to EndMT or the simple seeding of the wells with MSCs. Accordingly, we make no finding of manipulation with respect to the plates of cells that Dr. Medici purported to treat.

With respect to the plates of HDMECs that Ms. Ramirez was to treat with bleomycin, we reach a different conclusion. Critically, the evidence before us includes Ms. Ramirez's testimony that she never treated the cells. We found her testimony about her involvement with the April Experiments credible and compelling. Before the fact, she communicated her intention not to treat the cells to both Mr. Susienka and her sister, and her monitoring of the cells without ever adding bleomycin to them is documented by her meticulous lab notebook entries. (See discussion at Ex. 3C, pp. 86-87 [M. Ramirez].) At the time of the April Experiments, Dr. Medici believed that Ms. Ramirez had carried out his instructions. (Ex. 40, p. 5.) Indeed, it is his position, even after the revelation was made known to him during the course of this investigation, that he still "does not accept the representation [] that Ms. Ramirez actually did not treat her cells." (Id. at 6.) Dr. Medici reiterates this position in the Response at page 16, and again at page 29. He is not in a position, however, to speak to the point from firsthand knowledge. Ms. Ramirez is in such a position, and we believe she has done so honestly.

We are not dependent, however, solely on Ms. Ramirez's testimony to conclude that the HDMECs were untreated. Mr. Susienka, Ms. Ramirez, and Dr. Reginato all confirmed that bleomycin treatment causes extensive endothelial cell death. Dr. Reginato noted as "one of the major problems" of bleomycin treatment "that you can get about 80 percent cell death." (Ex. 3G, pp. 19-20 [Reginato], as amended.) When he was shown some of the images captured by

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Ms. Ramirez's before-and-after comparison photos (see Ex. 50), Dr. Reginato therefore found the proliferation of cells in the experimental wells, yielding more cells than had been plated, inconsistent with the possibility of bleomycin treatment. (Ex. 3G, pp. 21-22 [Reginato].) Separately, Dr. Reginato also made the point that of the cells that survive the bleomycin treatment, the percentage of transformation is not that high; noting that the results are "not uniform" he estimated transformations of only 10% or 20% of the endothelial cells. (Ex. 3G, p. 20 [Reginato].) And yet the image that Dr. Medici emailed Ms. Ramirez and the images she photographed show a profusion of well-formed mesenchymal cells in wells that had never been treated (see April 6 cells from plate wells labeled "for Treatment" in Exhibit 48).

As an alternative to an explanation dependent upon bleomycin treatment, Dr. Medici ventures the possibility that the mesenchymal morphologies observed in Ms. Ramirez's plates occurred spontaneously, that is, that EndMT took place without the action of any transforming agent. Only a short while ago, Dr. Medici would seemingly not have countenanced this theory. In his interview, when we believe he was still unaware that Ms. Ramirez had refrained from treating, Dr. Medici confirmed that an endothelial cell would not undergo EndMT without a transforming agent. (Ex. 3A, pp. 25-26 [Medici].) With specific reference to Ms. Ramirez's plates, Dr. Reginato made the same point. ³⁸ Dr. Medici rests his revised opinion entirely on the January 2015 article by Huang, L. et al., reporting on the conversion of endothelial cells to a mesenchymal phenotype. (See Ex. 51.) According to Dr. Medici, the research reported by Huang, et al., "demonstrated that EndMT can spontaneously occur in cell culture." (Ex. 40, p. 6.)

We believe Dr. Medici's point is untenable. First, the research procedures followed by Huang, et al., bear no resemblance to what occurred in the present case. As the journal article recounts, the researchers worked with a specially purified population of hemangioma endothelial cells, using antibody-coated magnetic beads at two stages to select cells that were positive for the glucose transporter 1 (GLUT1) protein. Moreover, the double-selected GLUT1+ cells underwent a total of three weeks of culture before they displayed a mesenchymal morphology. (Ex. 51, p. 138.) Contrast this to the undifferentiated HDMECs that remained in Ms. Ramirez's plates for, at most, four days (April 2 to April 6) before seeming to undergo a robust transformation to spindle-shaped cells. Second, Dr. Medici's theory of spontaneous EndMT would require us to believe that the phenomenon somehow occurred only in the bottom three wells of Ms. Ramirez's plates, while the top three control wells in each plate exhibited nothing.

In the end, we believe that the cells present in the bottom wells of the plates were not generated through the EndMT process but represented mesenchymal cells that were deliberately placed there, and we believe the preponderance of the evidence supports the conclusion that Dr. Medici – who had the knowledge, means, and opportunity to do so – was the individual who placed them there. We are satisfied that neither Diana, Melissa, nor Michael did so, and we have seen no basis to fabulate a third party who selected precisely these two plates apart from Dr.

Shown the before and after images in Exhibit 50, Dr. Reginato confirmed several times that the transformations in the latter images would have required the addition of a transforming agent. (Ex. 3G, pp. 22-24 [Reginato].)

Final Report of the Lifespan Investigation Committee August 18, 2015

Medici's other plates - not to mention Melissa's own plates of HUVECs - for manipulation.³⁹

The Investigation Committee concludes based on the evidence that Dr. Medici committed research misconduct as charged in Allegation 4. Specifically, the Investigation Committee has concluded by a preponderance of the evidence presented to it that Dr. Medici falsified an experiment conducted in his laboratory by manipulating the research materials used in the experiment such that the research is not accurately represented in the research record, and that such falsification was done intentionally. Furthermore, it is the Investigation Committee's conclusion that such intentional falsification represents a significant departure from accepted practices of the relevant research community.

VIII. CONCLUSION AND RECOMMENDATIONS

For the reasons discussed above, it is the recommendation of the Investigation Committee to the Lifespan Deciding Official that Dr. Medici be found by Lifespan to have committed research misconduct within the meaning of 45 C.F.R. Part 93 and the Lifespan Policy in connection with Allegations 1, 2 and 4. Dr. Medici's actions constitute serious breaches of the ethical standards of the Lifespan research community.

Because Dr. Medici's misconduct implicates unpublished manuscripts and research that had not yet been incorporated into any manuscript (i.e. the April Experiments), the Investigation Committee is unaware of any published article subject to these findings that requires retraction at this time. It is our understanding that prior submissions of the Walsh Manuscript to various journals were met with rejection and we are unaware of any outstanding publication determinations to be made regarding that paper. If Lifespan becomes aware of any additional active submissions of the Walsh Manuscript, a separate analysis would be required to determine if the version of the paper under consideration by the journal contains any falsified data or otherwise should be retracted from submission. We recommend that Lifespan consider notifying the co-authors of the Walsh Manuscript of the general findings related to Allegations 1 and 2, in order to ensure that any further use of the research reflected in the manuscript can be appropriately scrutinized. For similar reasons, we encourage notification of Dr. Reginato of the findings related to Allegation 4, given the suggestion in the evidence that the implicated experiment may have been intended to support on-going collaborative work between his and Dr. Medici's labs.

LIFESPAN INVESTIGATION COMMITTEE

Jonathan Kurtis, M.D., Ph.D. (Chair) Adam Chodobski, Ph.D. Loren D. Fast, Ph.D. Bharat Ramratnam, M.D.

Unlike the HDMECs, the HUVECs, treated with bleomycin by Ms. Ramirez on April 8, yielded no observable morphological changes at the 72-hour time-point recorded in her laboratory notebook on April 11. (Ex. 43, page numbered 114.)

Exhibit 4

Curriculum Vitae



Michael Susienka

EDUCATION

Brown University, Providence, RI

Ph.D., Biomedical Engineering, May 2017 Thesis Advisor: Jeffrey R. Morgan, Ph.D.

Thesis Title: Quantifying the fusion and self-assembly of 3D microtissue building parts

Worcester Polytechnic Institute, Worcester, MA

B.S., Biomedical Engineering (with High Distinction), May 2009 Minor in International Studies

PUBLICATIONS

Susienka MJ, Morgan JR. Principles of Fusion of Multicellular Spheroids. In Preparation.

Susienka MJ, Wilks BT, Morgan JR. 2016. Quantifying the Kinetics and Morphological Changes of the Fusion of Spheroid Building Blocks. Biofabrication 8(4): 045003. http://dx.doi.org/10.1088/1758-5090/8/4/045003.

Leary E, Curran S, Susienka MJ, Manning KL, Blakely AM, Morgan JR. Micro-molded Nonadhesive Hydrogels to Form Multi-cellular Microtissues – The 3D Petri Dish® In "3D Cell Culture: Technology and Application", Przyborski, S. (Ed.) Wiley-Blackwell, West Sussex, United Kingdom.

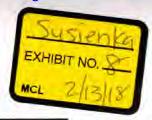
Susienka MJ, Medici D. 2013. Vascular endothelium as a novel source of stem cells for bioengineering. Biomatter 3(3): e24647. http://dx.doi.org/10.4161/biom.24647.

CONFERENCE ABSTRACTS

Susienka MJ, Cotoni K, Amara JP, Gillespie C. 2017. Clarisolve® mPAA Polymer: A Stimulus-Responsive Flocculation Polymer for Cell Culture Clarification. BioProcess International Conference & Exhibition. Boston, MA. Poster.

Ip BC, Cui F, Murphy J, Wilks BT, Manning KL, Susienka MJ, Bull C, Patterson WR. 2016. Biopick, Place, and Perfuse Instrument for Building Perfusable Large Proto-organs. TERMIS-Americas. San Diego, CA.

Ip BC, Cui F, Murphy J, Wilks BT, Manning KL, Susienka MJ, Bull C, Patterson WR. 2016. Biopick, Place, and Perfuse Instrument for Building Perfusable Large Proto-organs. Biofabrication. Winston-Salem, NC.



Susienka MJ, Morgan JR. 2015. A Quantitative, High-Throughput Platform for Investigating Fusion of Multicellular Spheroids. Biomedical Engineering Society Annual Meeting. Tampa, FL. Podium Presentation.

Susienka MJ, Walsh LA, Liang OD, Medici D. 2014. Identifying the molecular mechanisms by which synthetic triterpenoids induce chondrogenesis. Orthopaedic Research Society Annual Meeting. New Orleans, LA. Poster.

RESEARCH EXPERIENCE

MilliporeSigma, Bedford, MA

Research Scientist III, January 2017–present

Brown University, Providence, RI

Graduate Research Assistant, September 2011-December 2016

On Demand Therapeutics, Inc., Tyngsboro, MA

Engineering Consultant, April 2011-May 2011

MicroCHIPS, Inc., Bedford, MA

Biomedical Engineer, June 2009–December 2010

Genzyme Corporation, Framingham, MA

Summer Intern, June 2008-August 2008

LEADERSHIP & SERVICE

Webmaster, Brown University Graduate Biomedical Engineering Society, 2014–2015

Vice President, Brown University Graduate Biomedical Engineering Society, 2012–2013

Tour Guide, Crimson Key, WPI Office of Undergraduate Admissions, 2007–2009

Student Rep., Committee on Academic Operations, WPI Faculty Committee, 2008

Senator, WPI Student Government Association, 2007–2008

Chair, WPI Social Committee Executive Board, 2006–2008

Peer Mentor, WPI Student Support Network (Mental Health Awareness Group), 2007

SOFTWARE

Microsoft Office (Word, Excel, PowerPoint), ImageJ/Fiji, Adobe Acrobat, Adobe Photoshop, Adobe Illustrator, GraphPad Prism, R, SAS, Stata, CellProfiler, LaTeX, Zotero, EndNote, SolidWorks, Autodesk Fusion 360, Pro/ENGINEER, ANSYS, MATLAB, LabVIEW, MetroPro

TEACHING EXPERIENCE

Biomedical Engineering and Biotechnology Seminar, Fall 2016

Guest Lecturer

Full semester course (1 hour/week, 100 graduate students)

Guest Lecture Title: "The Science of Giving a Great Presentation"

Responsible Conduct in Research (RCR), Fall 2015

Teaching Assistant and Guest Lecturer

Half semester course (2 hours/week, 66 graduate students and post-docs)

Polymer Science for Biomaterials (BIOL 1090), Fall 2014

Teaching Assistant

Full semester course (3 hours/week, 20 undergraduate students)

Biomaterials (ENGN 1490), Fall 2013

Teaching Assistant and Guest Lecturer

Full semester course (3 hours/week, 40 undergraduate and graduate students)

Guest Lecture Topic: Tissue Engineering and Regenerative Medicine (1 hour)

Stem Cell Engineering (BIOL 1150), Spring 2013

Teaching Assistant and Guest Lecturer

Full semester course (6 hours/week, 20 undergraduate and graduate students)

Guest Lecture Topic: Data Analysis Workshop (1 hour)

Introduction to Stem Cells and Tissue Engineering (CEBI 0902), Summer 2012

Teaching Assistant

Summer course (2 weeks, 6 hours/week, 30 high school students)

AWARDS & AFFILIATIONS

Biomedical Engineering Society, 2015–2016

Orthopaedic Research Society, 2014–2015

Tau Beta Pi, National Engineering Honor Society, 2008

Alpha Eta Mu Beta, National Biomedical Engineering Honor Society, 2008

Dean's List, Worcester Polytechnic Institute, 2008–2009

Charles O. Thompson Award, Worcester Polytechnic Institute, 2006

TRAINING CERTIFICATES

USM/MeRTEC Research Integrity and Regulatory Compliance Symposium, May 2016

Exhibit 5



Rhode Island Hospital

A Lifespan Partner

July 17, 2012

Damian Medici 790 Boyiston Street Boston, Massachusetts 02199

Dear Damian:

I am pleased to offer you the position of Research Associate II at Rhode Island Hospital/Hasbro Children's Hospital. You will be an asset to the fine team of healthcare professionals who serve the people of Southern New England. I would like to confirm the following:

JOB SPECIFICS:

Position: Research Associate II Department: Orthopaedics

Unit: Orthopaedics
Manager: Dr. Ehrlich
Status: Full-time
Hours Per Week: 40.00

HUMBICI WCCK. T

Shift: Days

Work Schedule: to be determined

Rate of Pay: \$86.54 Pay Frequency: Hourly

Projected Start Date: July 23, 2012

*** Start Date is pending completion of background check and clearance from employee health services.

Hospital Orientation: July 23, 2012

***Held from 12:30pm to 5:00pm in Gerry House.

***Business casual attire or a uniform/scrubs is appropriate for Orientation.

The Hospital reserves the right to assign shifts, hours and overtime to meet its employment needs. Your first six months with Rhode Island Hospital are considered a probationary period; completion of this period does not guarantee continued employment. Your employment is also contingent upon receipt of eligibility to work in the United States, successful completion of a background check, completion of a satisfactory reference check, and successful completion of your pre-placement physical with Employee and Occupational Health Services.

If you have not done so already, please call Health Services at (401) 444-4038 to schedule your health screening. You should bring your completed immunization records from your physician with you the day of your scheduled appointment. Should you have any questions regarding your employment while working at Rhode Island Hospital, please contact your Human Resources Representative, Andrea Mansmann.

https://lifespan.taleo.net/servlets/art.product.recruiterwebtop.MainOperatorServlet?art_ip_... 7/17/2012

Page 2 of 2

If you understand and accept these terms, please sign and return a copy of this letter to our Human Resources Department. Rhode Island Hospital is an outstanding organization with capable, dedicated staff. We believe you will become a valuable, enthusiastic member of our team. Welcome to Rhode Island Hospital.

Sincerely,

Melli stad Prucipalo Melissa Principale

Recruiter

OFFER ACCEPTED: Damian Medici

Signature

 $\frac{7//9//2}{\text{Date}}$

Exhibit 6

Exhibits: 28-56 Volume 1, Pages 1-256

UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF RHODE ISLAND

DR. DAMIEN MEDICI,

Plaintiff,

vs. Civil Action No. 1:17-cv-00265-M-PAS

LIFESPAN CORPORATION et al.,

Defendants.

DEPOSITION OF DAMIEN MEDICI
Wednesday, February 14, 2018, 9:05 a.m.

Verrill Dana LLP

One Boston Place

Boston, Massachusetts

------Reporter: Alan H. Brock, RDR, CRR-----abrock@fabreporters.com www.fabreporters.com
Farmer Arsenault Brock LLC
50 Congress Street, Suite 350
Boston, Massachusetts 02109
617.728.4404 fax 617.728.4403

- Q. But they were not friends of yours.
- 2 A. No.

- Q. Were you applying for jobs at this time?
- A. Yes. I think I had actually applied for professorships for I'd say at least a few years prior to this. But as my mentors explained to me, applying for a faculty position was a complete waste of time because everything is done through recruitment, either by department chairs or by search committees.

It usually works that an academic institution or hospital will actually post a job posting after they've already decided who they want. In fact, that's what Lifespan did to me. When I arrived there in early July of 2012, they told me I couldn't officially be on the record as being an employee because they needed to post that they were searching for somebody for a period of three weeks before I could officially be an employee.

- Q. Were you recruited by any other institutions during this period in which you were applying for professorships while you were in -- at the dental school?
- 24 A. Yes.

- Q. And if you look at Page DM 886, that reflects that your total guaranteed salary is 180,000; is that correct?
 - A. Yes.

- Q. And that's consistent with what you understood the offer was initially when you began at Rhode Island Hospital?
 - A. For base salary, yes.
- Q. If you turn back to the first page of this document, Paragraph 2, you'll see the last sentence in that paragraph says, "All of Doctor's activities hereunder shall conform strictly to the standards of the department, hospital and Brown as applicable in effect from time to time and of the hospital staff association bylaws as applicable as in effect from time to time." Do you see that?
- A. Yes.
 - Q. What do you understand that to mean?
- A. Well, it's rather vague, so I'm not really sure how to characterize it. I assume it's referring to hospital policies.
- Q. What did you understand your obligations to be under that sentence?
 - A. I assume it refers to conforming with the

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1
    department and hospital's policies.
2
            So then you understood it was your
3
    obligation to conform with the department and the
    hospital's policies?
4
5
            From what I'm reading here, I assume that's
6
    what this means.
7
            Is that what you understand it to mean?
        Q.
8
            That's what I'm currently interpreting it
        Α.
9
    to mean.
10
            What do you think you understood it to mean
        Q.
11
    at the time you signed the agreement?
12
        Α.
            I don't remember what I was thinking at the
13
    time I signed this agreement. That was a long time
14
    ago.
15
            I'm not asking you to recall what you were
16
    thinking. I'm just asking what you understood it to
17
    mean at the time.
18
            I mean, it's rather vague, so....
19
                 I mean, I assume, as it states, conform
20
    with department and hospital policies.
21
            But those include policies on research
22
    integrity?
23
        Α.
          It doesn't say.
24
        Q.
            Based on your understanding, given that it
```

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72
    says "all the Doctor's activities shall conform
1
2
    strictly to the standards of the department,
3
    hospital, and Brown," do you think that included
    standards regarding research integrity?
5
        A. I assume that it would; I mean, any
6
    standard.
7
            Including research integrity standards?
        Q.
8
        Α.
            I assume so.
9
            Were you aware that Brown had a policy on
        Q.
10
    research integrity?
11
        Α.
            I was not familiar with Brown's policy on
12
    that.
13
            Are you aware that they had one?
14
            I would assume that they would have one.
        Α.
15
            And you understood that you were -- you had
        Q.
16
    an appointment at Brown as part of your employment
17
    by Rhode Island Hospital?
18
            Yes, I had a faculty position with Brown.
19
                MR. HARRINGTON: Can we take like a
20
    five-minute break?
21
                MS. WERTHEIMER: Sure.
22
                 (Recess taken.)
23
            Referring you back to Exhibit 36: If you
24
    would turn to Page 5 of that document, specifically
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136 we were just referring to: When was the last time you received any correspondence from Harvard relating to that investigation? Α. I think last summer. Do you have any information as to whether Q. and when they're going to be issuing a report of their investigation committee? Α. No. Is Mr. Harrington representing you with respect to that investigation? Α. I believe so. 12 Back to your time at Rhode Island Hospital: Q. 13 You were hired to establish a lab at Rhode Island 14 Hospital: is that correct? Α. Correct. 16 What did you do to establish that lab? Hired personnel, purchased equipment and 18 reagents, supplies, things like that. Who did you hire first? Q. Well, I don't know if it was considered an official hire, but the first person who joined the 22 lab was Michael Susienka, and he did a rotation in 23 the laboratory I'd say from August of 2012 until 24 maybe the end of that year.

Exhibits: 128-145 Volume 2, Pages 257-438

UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF RHODE ISLAND

Civil Action No. 1:17-cv-00265-M-PAS

DR. DAMIAN MEDICI,

Plaintiff,

VS.

LIFESPAN CORPORATION, et al.,

Defendants.

CONTINUED DEPOSITION OF DAMIAN MEDICI

Friday, May 4, 2018, 10:01 a.m.

Verrill Dana LLP

One Boston Place

Boston, Massachusetts

jty@fabreporters.com www.fabreporters.com

Farmer Arsenault Brock LLC

Boston, Massachusetts

617-728-4404

I searched through the computer that I currently have in my possession, which was acquired after I moved to Lifespan, for any work-related materials, which I believe my attorney sent to you, but I believe these are things that probably are already on either the laboratory computers at Lifespan or my office computer.

I don't know that for sure, but I would assume that's how they got on my personal computer, was from transferring them.

- Q. Did you look through those files to determine whether or not any of the files on that computer were responsive to the document request that I served in this litigation?
- A. Yes. My attorney and I both looked through, and as I stated, as far as I know, everything that has to do with the experiments and issue were already provided.
- Q. And that would be the approximately eight images that you provided to the Lifespan investigation committee?
- A. Yes, as well as the things that were sent -- excuse me; given to Harvard University as part of their investigation.

As far as I know, in terms of Lifespan's investigation, Allegations 1 and 2, those eight or nine images were the ones that had to do with the actual research in question.

And then Allegations 3 and 4 were things that should be on the computers at Lifespan.

- Q. Again, did you look through your files to determine whether you had any other files or documents that related to the research at issue in the Walsh manuscript?
- A. To my knowledge, the research at issue in the Walsh manuscript are what were in the allegations; and yes, I looked for that, and as far as I know, you've been provided all of that.
 - Q. Let me just clarify. Our document requests were specific. I asked for any documents or files related to any of the research.
 - A. Any of the research.
- Q. That was my request, at issue in the Walsh manuscript.
 - A. At issue, yes.

- Q. No, no; any of the research that was discussed in the Walsh manuscript.
 - A. Discussed in the Walsh manuscript?

267 1 MR. HARRINGTON: I agree with that. 2 Can we go off the record for a moment? 3 MS. WERTHEIMER: Yes. 4 (Discussion off the record) 5 MS. WERTHEIMER: Back on. 6 Dr. Medici, you also testified that at the 7 time that you left Harvard University, you had 8 brought with you certain pages of notebooks that you 9 had kept, lab notebooks that you had kept while you 10 were at Harvard. Do you recall testifying to that? 11 Α. Photocopies of pages, yes. 12 Q. Photocopies of pages. And during the first 13 day of your deposition, you testified you had not 14 reviewed those notebook page photocopies to 15 determine whether or not there were any pages that 16 related to the Walsh manuscript. 17 And my question for you is, have you 18 done so as you sit here today? 19 Well, I think there may be some things in 20 there that have to do with the Walsh manuscript. I 21 don't know off the top of my head, but I believe my 22 attorney sent you all the pages that I have in my 23 possession from that notebook. 24 MS. WERTHEIMER: 128.

291 Dr. Walsh. 1 2 Q. You don't recall whether one of you took 3 the first stab and the other one edited it, or vice 4 versa? 5 No, I don't recall. 6 Q. I believe you have previously testified 7 that the primary data, the source data, related to the research that is at issue in this manuscript was 8 9 left at Harvard. Is that correct? 10 Α. The original data, yeah. 11 Q. Well, other than the data that you showed 12 me that we discussed that was at Exhibit 39, those 13 cell images, is there other data in your possession 14 that relates to this research? 15 Not currently in my possession. Not that I 16 know of. I can double-check, like I said, and I 17 will. 18 Do you believe you took other data related Q. 19 to this manuscript with you when you left Harvard? 20 Α. Probably, yes. And then you just discarded at some point? 21 Q. 22 Α. No, I didn't discard it per se. 23 So why is it no longer in your possession? Q. 24 Well, I had two personal computers. I had Α.

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304
    there's a heading that says, "Being an author," and
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2
    then it says, "Responsibilities of senior team
3
    members." Do you see that?
        A. Yes.
            And it says, "The editors at the Nature
5
6
    journals assume that at least one member of each
7
    collaboration, usually the most senior member of
8
    each submitting group or team, has accepted
9
    responsibility for the contributions to the
10
    manuscript from that team." Do you see that?
11
        Α.
            Yes.
12
            And I believe you testified earlier that
        Q.
13
    you were the senior author on the Walsh manuscript?
14
        Α.
            Yes.
15
            It says here, "This responsibility
        Q.
16
    includes, but is not limited to, ensuring that
17
    original data upon which the submission is based is
18
    preserved and retrievable for reanalysis." Do you
19
    see that?
20
        A. Yes.
21
            Did you do that?
        Q.
22
        Α.
            Can you repeat that? I'm sorry.
23
        Q.
            Sure. Did you ensure that the original
24
    data upon which the submission was based was
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preserved and retrievable for reanalysis?

- A. Well, all the original data was back at Harvard, so it would have been preserved there, or it should have been.
- Q. Did you take any steps to ensure that that was preserved and retrievable?
- A. Like I said, some of the things I took or at least I had on my own personal computer; but it's my understanding that Harvard University should keep everything preserved. I don't think anybody is supposed to just get rid of stuff that's there. I think all the records, I think ultimately --

If somebody leaves the institution, then it's really the institution who has to preserve everything.

- Q. You could have taken copies of that data, could you not?
- A. I think I took -- I mean, I had copies of some things.
 - Q. Right. So you could have preserved the data that was related to the Walsh manuscript when you left Harvard; is that correct?
 - A. I suppose I could have.
 - Q. And in fact, as the senior author, you're

- Q. Dr. Medici, I'm handing you a document that was previously marked as Exhibit 44. If you'd turn to the second page of this document, does this look like the allegations that were the subject of Lifespan's research misconduct investigation?
 - A. Yes.

- Q. And turning to Allegation 4, are you familiar with this allegation?
 - A. I mean, I've read the allegation, yes.
- Q. Does this allegation relate to some work that you did in your lab at Rhode Island Hospital in or around April of 2014?
- A. Well, that's the interesting thing about the allegation. It doesn't say what experiment it's referring to. It's very vague.

But it's my understanding that this allegation, or at least what I eventually learned, that this allegation had to do with Melissa Ramirez's experiment at Rhode Island Hospital.

- Q. Did you do some work in your lab at Rhode Island Hospital in or around April of 2014?
- A. I did some troubleshooting tests in the label lab, yes.
 - Q. Had you done any work in the lab

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333 previously, your own experiments or tests in the lab? Α. My own? No. Q. So that was the first time that you did any experiments or tests in your lab at Rhode Island Hospital? Α. To the best of my recollection, yes. What was the purpose of those tests? Q. Well, I primarily went into the lab to try to figure out what Michael Susienka was doing wrong. He kept telling me that his experiments were failing, which didn't make much sense to me, especially since what he was studying was such a well-known and well-published mechanism. It's one of the most basic processes in biology, supported by thousands of publications stretching back to 1975. So I went into the lab to try to figure out whether there was an issue with his technique or whether there was an issue with the protocol, because I believe they were using different cells than I had used in the past, or my previous lab had used. So I didn't know whether or not we needed to adjust concentrations of drugs or

Exhibit 7

RIH / Research Ph.D. with F/T Academic Appointment (no clinical activities)

EMPLOYMENT AGREEMENT

THIS AGREEMENT made and subscribed as of this first day of January, 2014, by and between Rhode Island Hospital, a not-for-profit corporation organized under the laws of the State of Rhode Island ("Hospital"), whose sole member is Lifespan Corporation ("Lifespan"), and Damian Medici, Ph.D., a research scientist ("Doctor").

NOW, THEREFORE, in consideration of the promises and of the mutual covenants herein contained, the receipt and sufficiency of which are hereby acknowledged, the parties do hereby covenant and agree as follows:

1. Term. This Agreement and Doctor's employment hereunder as research scientist shall be effective from <u>January 1, 2014</u> through <u>June 30, 2019</u>. In the case of a Doctor who holds a full-time academic appointment at the Brown University School of Medicine ("Brown"), the term of the Agreement shall be concurrent with the term of such appointment, and evidence of such appointment shall be attached to this Agreement as Exhibit A.

As Doctor's position is supported by University Orthopedics, Inc., or as an alternative, the RIH Orthopedic Foundation, evidence of such support shall also be attached as Exhibit D.

2. Activities and Compensation. Doctor shall devote his/her full-time professional effort to employment in Hospital's **Department of Orthopedics** (the "Department"). Hospital expects such effort to total no less than 40 hours per week, which hours shall be allocated prospectively to the employment activities listed below corresponding approximately to the stated time allocations. Actual time spent by Doctor undertaking each activity shall be recorded and reported by Doctor pursuant to Section 6.2 herein. All of Doctor's activities hereunder shall conform strictly to the standards of the Department, Hospital and Brown, as applicable, in effect from time to time, and of the Hospital's Staff Association Bylaws, as applicable, as in effect from time to time.

Activity	Monthly Time Allocation (projected)
Administration Teaching Research	5 % 3% 92 %
Total	100%

~1~

RIH/Research Ph.D. (no clinical activities) F/T Academic Appt Damian Medici, Ph.D. 2014 - 2019 In consideration of all Doctor's services provided under this Section 2, Hospital shall pay Doctor an annual research salary as set forth on Exhibit B, payable in accordance with the Hospital's payroll policies in effect from time to time.

- approximately that time allocated to "Administration" to those activities related to the general benefit and welfare of all patients, Lifespan and the Hospital including, but not limited to: (i) supervision of technical and non-professional personnel when unrelated to direct patient care, (ii) education of hospital community members not enrolled in formal educational programs, (iii) service on Lifespan, Hospital and Departmental committees, and (iv) participation in Lifespan, Hospital and Departmental planning, budgeting and policy development. Assignment and scheduling of specific administrative activities shall be made and modified by Chief of the Department or designee ("Chief") from time to time.
- 2.2 Teaching Activities and Compensation. Doctor shall devote approximately that time allocated to "Teaching" to those activities furthering Lifespan and/or Hospital-related educational programs including, but not limited to: (i) education and supervision of interns, residents and fellows, (ii) planning, implementing and presenting seminars and conferences for approved educational programs, and (iii) undertaking administrative duties related to approved educational programs. Assignment and scheduling of specific teaching activities shall be made and modified by Chief from time to time, but will not exceed 5 10% of time allocation.
- 2.3 Research Activities and Compensation. Doctor shall devote approximately that time allocated to "Research" to participating as director, investigator and/or staff in one or more scientific research programs as such participation is approved by Chief in his/her sole discretion. These duties may include supervision of research staff members.
- 2.4 <u>Periodic Review</u>. Chief shall conduct a periodic review of Doctor's performance. Total compensation of Doctor will be in accordance with Hospital compensation guidelines in effect from time to time (unless approved otherwise by Hospital).

3. Activity Reallocation.

If at any time during the term of this Agreement, Chief determines that the prospective time allocations set forth in Section 2 require modification to meet the best interests of Lifespan, the Hospital and/or Department, Chief may propose to revise such allocations. Any such revision shall become effective thirty (30) days upon mutual agreement between Chief and Doctor.

4. <u>Benefits Package</u>. Hospital shall provide Doctor with the standard Hospital fringe benefit package then in effect from time to time. To the extent Doctor is providing

services to the Hospital hereunder on a part-time basis, such benefits shall be provided on a pro-rated basis in accordance with Hospital policy.

4.2 <u>Vacation</u>. Doctor shall be entitled to an amount of vacation time as determined by the standard Hospital fringe benefit package in effect during this agreement.

5. Termination.

- 5.1 <u>Upon Notice</u>. Doctor may terminate this Agreement upon a minimum of ninety (90) days' written notice to Chief / Chairman of the Brown department in which Doctor maintains his/her appointment and Hospital's Senior Vice President of Research. Doctor acknowledges that termination of this Agreement may, at the discretion of Brown, result in termination of his/her Brown appointment.
- 5.2 For Cause. (a) Hospital may terminate this Agreement at any time for cause upon delivery of written notice to Doctor. Hospital shall have cause for termination if Doctor is subject to any of the following defaults and such default continues for a period of fifteen (15) days after receipt of written notice from Hospital stating the specific default. Defaults shall include:
 - (i) if applicable, the revocation, suspension or limitation of the Doctor's license to practice in the State of Rhode Island or in any other state;
 - (ii) if applicable, the revocation, suspension or limitation of Doctor's Staff Association membership or Hospital privileges;
 - (iii) if applicable, the revocation, suspension or limitation of Doctor's right to participate in the Medicare or Medicaid programs or any managed care program which accounts for greater than fifteen percent (15%) of Hospital's gross revenues;
 - (iv) the Doctor being found to have participated in professional misconduct or to have been found professionally incompetent by any governmental entity or professional organization having jurisdiction;
 - (v) the Doctor's material violation of any of the terms of this Agreement;
 - (vi) termination by Doctor or Brown of the Doctor's Brown appointment; or
 - (vii) the Doctor's retirement, legal incompetency, repeated or untreatable substance abuse or total and/or permanent disability.

(b) Hospital may terminate this Agreement for cause upon delivery of written notice to Doctor after Doctor's failure (after reasonable notice and opportunity to cure from Hospital) to satisfactorily perform his/her administrative, teaching or research duties as required by Hospital / Department, to provide competent educational services or to treat patients, colleagues, Hospital staff or others in a satisfactory, professional manner and/or with requisite competence as to affect patient safety or quality of care.

6. General Duties.

- 6.1 Patient Records. All patient records shall be and shall remain Hospital's property.
- 6.2 <u>Time Allocation Reports</u>. Doctor shall prepare a monthly report indicating time spent on research activities to be submitted to the Hospital Office of Research Administration pursuant to said office's specified time frame. Such reports shall be submitted on a timely basis. Failure to timely prepare time allocation reports when due may result in Hospital's withholding all or part of Doctor's compensation until such reports are submitted.

7. Miscellaneous.

that the compensation and benefits received under this Agreement shall satisfy and discharge in full all of his/her claims upon Hospital for compensation in respect to his/her services rendered hereunder. Doctor understands that all his/her external grant funding will be received and administered by the Hospital; all direct funding allocations will be made by Doctor, provided they are consistent with general operating policies of the Hospital. Doctor acknowledges that his/her service in the employ of Hospital does not confer upon him/her any ownership interest in or personal claim upon any reimbursement expected by Hospital for his/her teaching, administrative and research activities, whether the same are collected during employment or after the termination thereof, and assigns all such fees and payments to Hospital. He/she hereby disclaims and renounces any such interest or claim.

Operatment Chief, Doctor shall apply to the Hospital's Staff Association for membership and privileges. Should said application be denied, this Agreement shall terminate upon the conclusion of the final review availed of by Doctor under the Staff Association bylaws. Nothing in the Agreement guarantees Doctor Staff Association membership or privileges.

Termination of this Agreement for any reason shall automatically terminate Doctor's Staff Association membership and privileges. With respect to any termination of Staff Association membership or privileges resulting from the termination of this Agreement, any rights that Doctor may have to any hearing or appeal procedures prior to

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termination of Staff Association membership or privileges, pursuant to the bylaws or policies of Hospital or its Staff Association, the Health Care Quality Improvement Act of 1986, or any other state or federal statute, regulation or judicial decision are hereby waived. In the event of any conflict between the terms of this Agreement and the Staff Association bylaws or policies of the Hospital, this Agreement shall be controlling.

- Disclosure of Confidential Information. Doctor agrees that during 7.3 and after his/her employment with Hospital he/she will not, without prior written consent from Hospital, disclose to others any trade secrets or confidential information obtained, received or created by Doctor during his/her employment. Nor, upon termination of his/her employment hereunder, shall Doctor take or otherwise carry away or use in any manner any trade secrets or confidential information. For purposes of this Agreement, trade secrets and confidential information shall mean any and all confidential and proprietary information of Hospital, including but not limited to financial information, business plans, expansion plans or proposals, strategic plans, pricing and marketing information, personnel data, patient or client lists, client intake forms, policies, procedures, case records, case histories, x-ray film or any other documents or materials pertaining to the business of Hospital or its dealings with patients. Trade secrets may also include, but not be limited to, confidential material provided by a research sponsor(s) or co-investigator(s), pending patent applications or disclosures, licensed technology or other intellectual property.
 - 7.4 Hospital Policies and Procedures: Corporate Compliance Plan.

 Doctor agrees to abide by and adhere to the requirements and obligations of all of
 Lifespan's and Hospital's policies and procedures in effect from time to time, including,
 without limitation, Intellectual Property and Conflict of Interest policies attached hereto
 as Exhibit C and made a part hereof. The requirements and obligations of the Intellectual
 Property and Conflict of Interest policies shall survive this Agreement's termination or
 expiration.

Doctor hereby certifies that he/she has reviewed and is familiar with the Lifespan Corporate Compliance Plan, a copy of which has been made available to Doctor. Doctor agrees to fully comply with the Corporate Compliance Plan at all times during the term of Doctor's employment with the Hospital.

- 7.5 Entire Agreement. This Agreement constitutes the entire understanding and, unless contemplated by specific provisions herein, agreement between Hospital and Doctor with regard to all matters herein. This Agreement supersedes in the entirety any and all previous agreements, whether written or oral, between the parties relating to the subject matter hereof.
- 7.6 Invalidity. If any provision of this Agreement shall be held, be deemed or shall in fact be, invalid, inoperative or unenforceable as applied to any particular case in any jurisdiction or jurisdictions or in all jurisdictions or in all cases, because of the conflict of any provision with any constitution, statute, rule of public policy, regulation, ordinance or for any other reason, such circumstances shall not have

the effect of rendering the provision or provisions in question invalid, inoperative or unenforceable in any other jurisdiction or in any other case or circumstance or of rendering any other provision or provisions herein contained invalid, inoperative or unenforceable to the extent that such other provision or provisions are not themselves actually in conflict with such constitution, statute, rule of public policy, ordinance or regulation but this Agreement shall be reformed and construed in any such jurisdiction or in such case as if such invalid, inoperative or unenforceable provision had never been contained herein and such provision performed so that it would be valid, operative and enforceable to the maximum extent permitted in such jurisdiction or in such case.

7.7 Assignability. In the event that Hospital merges with, or is consolidated into, any other corporation(s) or in the event it sells or transfers substantially all of its assets to another corporation, the terms of this Agreement shall inure to the benefit of, and be assumed by, the corporation resulting from such merger or consolidation or to which the Hospital's assets shall be sold and transferred.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement, inclusive of the Appendix, as of the day and year first above written.

DOCTOR:

By: Damian Medici, Ph.D.

HOSPITAL:

Michael G. Ehrlich, M.D.

Chairman

Department of Orthopaedics

Brown University

Chief

Department of Orthopedics

Rhode Island Hospital

Peter J. Snyder, Ph.D.

Senior Vice President, Research

Lifespan

EXHIBIT A

FACULTY APPOINTMENT LETTER from Brown University.

[to be attached when finalized]

Mann of the

Signature:

Damian Medici, Ph.D.

EXHIBIT B

COMPENSATION for YEARS - 1-4

(Reference in () is made to the relevant Section of the Employment Agreement)

NOTE: Year 1 is the period January 1, 2014 through June 30, 2019.

Administrative Activities (§2.1)

Teaching Activities (§2.2)

Research Activities (§2.3)

Total Guaranteed Salary \$ 180,000 (1), (2), (3)

- (1) Funding sources for salary (in the order applied):
 - Grant salary support
 - Funding from University Orthopedics, Inc., or alternatively, RIH Orthopedic Foundation
- (2) See also information below regarding Additional Compensation Potential.
- (3) Base salary will be increased the usual and customary hospital-wide annual increases in subsequent years, upon approval by Chief.

Base Salary (as a component of Total Salary) for purposes of Doctor's Brown University academic appointment (Exhibit A):

\$ 180,000

Signature:

Damian Medici, Ph.D.

RIH/Research Ph.D. (no clinical activities)

F/T Academic Appt

Damian Medici, Ph.D. 2014 - 2019 EXHIBIT B (continued)

COMPENSATION

ADDITIONAL COMPENSATION POTENTIAL:

1) In addition, for each dollar of his salary Doctor covers through direct external research grant salary support (e.g. not reimbursed by funds from the RIH Orthopedic Foundation, Inc. or University Orthopedics, Inc.) that Doctor receives or from restricted funds previously generated by Doctor, twenty-five cents on the dollar will be paid in the form of a bonus to Doctor, to be paid in two equal installments, one in January and one in June. This bonus opportunity is capped at a maximum of \$45,000 in a given calendar year. This money may be used by the Doctor to pay a research technician or as additional salary bonus.

EXHIBIT C

INTELLECTUAL PROPERTY POLICY AND CONFLICT OF INTEREST POLICY

[see attached copies]

CORPORATE COMPLIANCE PLAN

[copy available for review from Chief - please arrange to review before beginning employment]

Damian Medici, Ph.D. 2014 - 2019 Signature:

Damian Medici, Ph.D.

EXHIBIT D

EXPECTATIONS AND PERFORMANCE CRITERIA; REAPPOINTMENT CRITERIA

I EXPECTATIONS AND PERFORMANCE CRITERIA

Doctor will use his/her best efforts to achieve the following during the term of the initial contract beginning January 1, 2014:

- Develop and maintain and/or collaborates on an externally funded laboratory program which funding
 includes significant support towards Doctor's personal compensation amount as set forth in this
 contract, a large majority of the laboratory's operating expenses and contributions to laboratory
 overhead.
- 2) Establish a high quality research program as evidenced by peer-reviewed publications in professional journals including, but not limited to, The Journal of Bone and Joint Surgery and The Journal of Orthopaedic Research. Other intellectual work, including reviews, chapters, abstracts, presentations at national meetings and invited lectures are considered of great value.
- Participation in national organizations including, but not limited to, study sections, the Orthopaedic Research Society and other professional organizations, editorial boards, etc.
- 4) Participation in Departmental educational programs for students and residents. This includes participation in weekly Departmental research conferences and Basic Science conferences, and advising on students and resident research programs.
- 5) Maintain collegial and supportive interpersonal relationships within the Department and University. Assist other investigators in the laboratory and collaborate on projects of mutual interest. Support the Department chairman in his academic and education commitments.
- 6) Participation in the activities of a Basic Science department on the Brown University campus is desirable.
- 7) The quantity and quality of professional activity will equal that of peers in the top one third of orthopedic departments nationally. This will be determined, if necessary, by using data generated by nationally recognized organizations such as the American Academy of Orthopaedic Surgeons, the Academic Orthopaedic Society and the Residency Review Committee.

EXHIBIT D

LETTER OF SALARY SUPPORT AND GUARANTEE FROM

University Orthopedics, Inc.

Exhibit 8

Lifespan System-wide Policy

Subject:

File under: Lifespan Policy on Research

Misconduct

ORA GEN 005

Issuing Department:

Research Administration -

Lifespan

Latest revision date:

October 15, 2012

Original Policy Date:

January 14, 1997

Approved by:

Administrative Director

Peter J. Snyder, Ph.D. Senior Vice President for Research, Chief Research

Officer

Purpose:

To provide an appropriate policy and related procedures regarding the investigation and reporting of possible Research Misconduct, as defined herein, and to comply with the current federal regulatory requirements applicable to research.

I. INTRODUCTION

A. General Policy

In all scientific and research activities, Lifespan expects the individuals performing research to observe the highest standards of honesty and professional conduct. It is integral for the enterprise of scientific and medical research to maintain the trust and confidence of both the scientific community and the public at large in the integrity of the scientific process. Unethical behavior represents a breach of confidence among scientists and researchers. It also undermines the confidence of the public and research subjects in the reliability of science and medicine. For these reasons, Lifespan considers Research Misconduct to be a betrayal of fundamental medical and scientific principles and shall promptly deal with all instances of possible research misconduct according to the procedures set forth in this policy.

It is the goal of Lifespan to recognize when Research Misconduct undermines the integrity of the scientific process and of the research enterprise. This policy was developed to prevent, detect, and redress Research Misconduct in Lifespan research programs. This policy aims to handle allegations of research misconduct swiftly and effectively, while also providing due process and fairness for those whose conduct is questioned.

B. Scope and Application

This policy and the associated procedures apply to all research activities conducted under the auspices of Lifespan, regardless of funding source. This policy applies to any person involved in research who is paid by, under the control of, or affiliated with Lifespan, such as physicians, scientists, trainees, technicians and other staff members, students, fellows, guest researchers, volunteers or collaborators at Lifespan. In addition, these policies and procedures apply to all individuals utilizing any Lifespan Institutional Review Board ("IRB") or other Lifespan research review committee for review and monitoring of research projects, regardless of whether the individuals are employed by, under the control of, or formally affiliated with Lifespan.

This policy and associated procedures will normally be followed when a Lifespan official receives an Allegation. Particular circumstances in an individual case may dictate variation from the normal procedure when it is deemed to be in the best interests of research integrity, or as needed for the operations of Lifespan and/or of any relevant federal agency. Any change from normal procedures must ensure fair treatment to the subject of the Inquiry or Investigation. Any significant variation from this policy and associated procedures shall be made only in consultation with the Office of General Counsel at Lifespan.

Research Misconduct and/or Retaliation occurring more than six years prior to submission of the allegations will not normally be investigated, unless there is compelling reason to do so. For example, an investigation may be warranted notwithstanding the lapse of more than six years when circumstances indicate (i) that the alleged Research Misconduct was not reasonably discoverable at an earlier time; (ii) that the Respondent has continued or renewed any incident of alleged Research Misconduct that occurred before the six-year limitation; or (iii) that the Research Misconduct poses a current threat to the health and safety of patients, staff, and/or employees.

II. DEFINITIONS

- A. Allegation means any written or oral statement or other indication of possible Research Misconduct made to a Lifespan official, including to a member of the IRB or other research review committee.
- Complainant means the individual(s) who submits an Allegation and/or a claim of Retaliation.
- C. Deciding Official means the Lifespan official who makes final determinations on Research Misconduct proceedings and any responsive Lifespan actions. At Lifespan, the Deciding Official is the Executive Vice President for Physician Affairs (Contact Phone: 401-444-5074).

- D. Good Faith Allegation means an Allegation made with the honest belief that Research Misconduct may have occurred. An Allegation is not in good faith if it is made with reckless disregard for, or willful ignorance of, facts that would disprove such Allegation.
- E. Inquiry means gathering information and initial fact-finding to determine whether an Allegation or apparent instance of Research Misconduct warrants an Investigation.
- F. Investigation means the formal examination and evaluation of all relevant facts to determine if Research Misconduct has occurred and, if so, to determine the responsible person and the seriousness of the Research Misconduct.
- G. ORI means the Office of Research Integrity, the office within the U.S. Department of Health and Human Services ("DHHS") that is responsible for the research misconduct and research integrity activities of the U.S. Public Health Service ("PHS").
- H. Research means a systematic experiment, study, evaluation, demonstration, or survey designed to develop or contribute to general knowledge (basic research) or specific knowledge (applied research) relating broadly to public health by establishing, discovering, developing, elucidating, or confirming information about, or the underlying mechanism relating to, biological causes, functions, or effects, diseases, treatments, or related matters to be studied. Research includes the development of individual patient case reports.
- I. Research Misconduct means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. It does not include honest error or honest difference in interpretation or judgment of data, or of regulatory and ethical standards.

A finding of Research Misconduct made under this policy requires that: (1) there be a significant departure from accepted practices of the relevant research community; and (2) the misconduct be committed intentionally, knowingly, or recklessly; and (3) the allegation be proven by a preponderance of the evidence.

Good Faith Allegations that describe problematic conduct that does not rise to the level of Research Misconduct will be handled in accordance with Section III.C of this policy.

¹ Fabrication means making up data or results, and recording or reporting them. Falsification means manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record. Plagiarism means the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

- J. Research Integrity Officer means the Lifespan official responsible for assessing Allegations and determining when such Allegations warrant Inquiries and for overseeing Inquiries and Investigations. The Senior Vice President for Research/Chief Research Officer is the Research Integrity Officer for Lifespan (Contact Phone: 401-444-4117).
- K. Respondent means the person against whom an Allegation or claim of Retaliation is directed or the person whose actions are the subject of an Inquiry or Investigation. There can be more than one Respondent in any Inquiry or Investigation.
- L. Retaliation means any adverse action taken against an individual by Lifespan or a Lifespan employee or staff member in response to a Good Faith Allegation of Research Misconduct made by the individual or in response to good faith cooperation with Research Misconduct proceedings at Lifespan.

III. GENERAL POLICIES AND PRINCIPLES

A. Reporting Misconduct

Individuals employed by or associated with Lifespan should, in general, report suspected Research Misconduct to the Research Integrity Officer. A Complainant who is not comfortable bringing his or her concerns to the Research Integrity Officer may direct those concerns to any responsible official of Lifespan, who is then required to direct the Allegation to the attention of the Research Integrity Officer. All conversations between the Complainant and the Research Integrity Officer or other responsible official will be handled confidentially, to the extent allowed by law.

If an individual is unsure whether a suspected incident falls within the definition of Research Misconduct, he or she may call the Research Integrity Officer to discuss the suspected misconduct informally. The individual must be informed, however, that if the Research Integrity Officer determines that an investigation of Research Misconduct is warranted, that official must submit an Allegation even if the individual chooses not to do so.

If the Research Integrity Officer believes the circumstances described by the Complainant do not meet the definition of Research Misconduct, the Research Integrity Officer will explain this to the Complainant and, as appropriate, may refer the Complainant or allegation to other offices or officials who might be helpful in resolving the problem, as further described in Section III.C. of this policy. If the Complainant disagrees with the Research Integrity Officer's opinion, the Complainant may still submit an Allegation and it will be duly considered. If the Research Integrity Officer believes the circumstances described do or may constitute Research Misconduct, he or she will advise the Complainant about how to make a formal Allegation.

B. Protection of the Complainant, Respondent, and Others

The rights and reputation of all parties involved in the Allegation, including the Complainant, must be protected throughout these procedures. Disclosure of the identities of the affected individual(s)

shall be limited, to the extent possible and except as otherwise required by law, to those who need to know such identities and/or related information in order for a thorough, competent, objective, and fair Research Misconduct proceeding to be conducted. In addition, confidentiality must be maintained for any records or evidence from which research subjects might be identified; except as otherwise required by law, disclosure is limited to those who need to know to carry out the Research Misconduct proceedings.

It is Lifespan's policy that no one shall suffer Retaliation for making a Good Faith Allegation, or for providing evidence or testimony regarding the facts and circumstances surrounding alleged Research Misconduct during an official Inquiry or Investigation. Regardless of whether Lifespan or ORI ultimately determines that Research Misconduct occurred, the Research Integrity Officer will monitor the treatment of individuals involved in Research Misconduct proceedings and will undertake reasonable efforts to protect a Complainant who made a Good Faith Allegation and others who cooperated in good faith with Inquiries and Investigations, including, but not limited to, all witnesses and committee members. Upon completion of an Inquiry or Investigation, the Deciding Official will determine, after consulting with the Complainant, what steps, if any, are needed to restore the position or reputation of the Complainant. The Research Integrity Officer is responsible for implementing any steps that the Deciding Official approves.

Research Misconduct proceedings will be conducted in a manner that will ensure fair treatment to the Respondent(s) in thoroughly carrying out the Inquiry or Investigation, and shall ensure confidentiality to the extent possible without compromising public health and safety. Respondents accused of Research Misconduct may consult with legal counsel, or a non-lawyer personal advisor (who is not a principal or witness in the case) to seek advice and, with notice to the Research Integrity Officer, may bring the counsel or personal advisor to interviews or meetings on the case. However, such counsel or personal advisor may provide passive assistance only to their client during official Research Misconduct proceedings, and may not participate in actual examination or cross-examination of witnesses.

C. Problematic Conduct That Does Not Qualify as Research Misconduct

The Research Integrity Officer will evaluate each Allegation to see if it purports to identify actions that would or might constitute Research Misconduct. In cases where the substance of an Allegation does not rise to the level of Research Misconduct but involves other problematic conduct, Lifespan and the Lifespan hospitals will take such conduct very seriously and will make a decision about how best to investigate and redress it. Examples of problematic conduct that might not rise to the level of Research Misconduct but are none-the-less very serious, include but are not limited to: intentional or reckless disregard of or significant and substantial departure from accepted research practices, applicable federal regulations, Lifespan policies, IRB directives on the appropriate and ethical conduct of human subjects research, or recognized research ethics; or, the submission of research forms or documents required by study sponsors that contain intentional or reckless material misstatements or omissions; or, falsification of academic or professional credentials.

If the Research Integrity Officer, in consultation with the Office of the General Counsel, decides not to handle a particular instance of problematic conduct as Research Misconduct, the matter may be referred to the applicable IRB or other research review committee, as appropriate, or to other appropriate forums within Lifespan or the Lifespan hospitals; outside consultants may also be

engaged to assist with such matters, at Lifespan's discretion. On a case-by-case basis, Lifespan also reserves the right to employ the procedures in this policy to address problematic conduct that does not qualify as Research Misconduct.

Past precedent in the handling of particular types of problematic conduct shall not be construed to be any form of guarantee or assurance as to the way future instances of problematic conduct will be handled.

D. Role of the IRB in Problematic Conduct Involving Research with Human Subjects

If an Allegation implicates research involving human subjects, the Research Integrity Officer must consult with the Office of General Counsel and the IRB Chair to determine whether the Allegation(s) should be handled by the IRB and its representatives, should be directed into the Research Misconduct process, or should be handled jointly by the IRB and Lifespan. If at any point in a Research Misconduct proceeding, the Research Integrity Officer determines that conduct in an Allegation does not constitute Research Misconduct, but raises concerns about the protection of human subjects in research, then the Allegation will be referred to the IRB for investigation and resolution of these matters. If, in the course of IRB duties, any IRB member becomes aware of conduct that might constitute Research Misconduct, the Chair of the IRB will similarly consult with the Research Integrity Officer and with the Office of General Counsel.

If it is determined by the Research Integrity Officer in consultation with the Office of General Counsel and the IRB Chair that an Allegation should be handled primarily by the IRB, such matter shall be handled in accordance with the IRB policy regarding Non-Compliance in the Conduct of Human Subjects Research. Pursuant to this policy, the IRB may employ any reasonable means of pursuing the investigation and resolving the matter, and for this purpose, may call upon research staff, members of the medical staff, the Office of General Counsel, or outside consultants or attorneys, for assistance. All such persons who assist for this purpose shall have full access to the relevant research materials and medical records, as an agent of the IRB itself, and all researchers and staff members of Lifespan are expected to cooperate in any such process. At the end of the process, the IRB, in consultation with the Research Integrity Officer and the Office of General Counsel, will determine whether a violation of policies, procedures, regulations or research ethics has occurred. The IRB will then specify appropriate corrective actions (e.g., disclosure to subjects, reconsent of subjects) and may impose sanctions (e.g., temporary or permanent suspension of research at issue or of other research activities, mandatory research skills retraining). All Lifespan staff and employees are expected to comply with such determinations.

IV. PROCESS FOR HANDLING ALLEGATIONS OF RESEARCH MISCONDUCT

A. Summary of the Research Misconduct Process

Once an Allegation has been made, and once the Research Integrity Officer, in consultation with the Office of General Counsel, has determined that the Allegation purports to identify actions that constitute Research Misconduct and that the Allegation is sufficiently credible and specific enough so that potential evidence of Research Misconduct may be identified, then the following procedures will be undertaken: (i) submission of the Allegation and initial Inquiry; (ii) when warranted, an

Investigation to collect data and thoroughly examine the evidence; and, (iii) issuance of formal findings and appropriate disposition.

If at any time during the Inquiry or Investigation, information is obtained that reasonably indicates the occurrence of possible criminal violations, the Research Integrity Officer must notify the Office of General Counsel of the specific facts within 24 hrs. In consultation with the Office of the General Counsel, the Research Integrity Officer, as necessary, will then promptly inform the appropriate office of the sponsoring or funding entity; ORI, if applicable; and the appropriate law enforcement officials. If reporting to ORI is applicable, ORI must also be notified promptly if any of the following conditions exist: (i) if there is an immediate health hazard involved, including a risk to human or animal subjects; (ii) if there is an immediate need to protect the interests of the Complainant(s) or the Respondent(s) or their co-investigators and associates; (iii) if there is an immediate need to protect federal resources or interests; (iv) if research activities should be suspended; (v) if it is probable that the alleged incident will be reported publicly; or, (vi) if the research community or public should be informed. Additional reports shall be made as required under Lifespan's Federalwide Assurance (FWA) and applicable federal, state, and local law.

Lifespan employees and Lifespan's medical staff are required to participate in any Research Misconduct proceedings, including reporting Allegations of Research Misconduct as necessary, and participating in meetings and answering questions put to them, upon reasonable notice, to facilitate investigations of Research Misconduct. Employees have an obligation to provide relevant evidence concerning Allegations to the Research Integrity Officer or other Lifespan officials, and all agents and representatives of Lifespan with respect to the proceedings have the right to examine research and medical records relevant to the Allegations. If others subject to this policy refuse to cooperate with these procedures, Lifespan will deal with this strongly, up to and including disassociation of Lifespan from research projects; revocation of all Lifespan support and/or approval; and reporting to government authorities, as required and applicable.

B. Submission of an Allegation

After consulting with the Research Integrity Officer, a Complainant may submit an Allegation to the Research Integrity Officer, or the Research Integrity Officer may record an Allegation based on information obtained from a Complainant. Upon receiving or recording an Allegation that purports to implicate Research Misconduct and that is sufficiently credible and specific enough so that potential evidence of Research Misconduct may be identified, the Research Integrity Officer will promptly select an <u>ad hoc</u> committee to conduct an Inquiry (the "Inquiry Committee"). The Research Integrity Officer shall take steps to ensure that individuals selected to serve on the Inquiry Committee do not have unresolved personal, professional, or financial conflicts of interest with the Respondent, Complainant, or essential witnesses.

C. Inquiry

The Research Integrity Officer will prepare a charge for the Inquiry Committee that describes the Allegations and any related issues identified during the Allegation assessment and that states that the purpose of the Inquiry is to make a preliminary evaluation of the evidence and testimony of the Respondent, Complainant, and key witnesses to determine whether there is sufficient evidence of possible Research Misconduct to warrant an Investigation. The purpose of this Inquiry is not to

determine whether Research Misconduct definitely occurred or who was responsible; rather, it is to determine whether more substantial Investigation is warranted. Thus, an Inquiry does not require a full review of all the evidence related to the Allegation. Inquiry by the committee shall begin promptly after the charge is received. The Research Integrity Officer should notify the Respondent(s) of the initiation of the Inquiry, and of the names of the individuals solicited to serve on the Inquiry Committee. The Respondent may raise objections (e.g., concerns about conflicts of interest) to the individuals on the Inquiry Committee in writing within seven working days of the receipt of this notification, and the Research Integrity Officer shall consider these objections. The Research Integrity Officer shall also notify the Department Chair, Division Chief, and/or Laboratory Director of the Allegations and Inquiry, as appropriate.

The Inquiry Committee will normally interview the Complainant, the Respondent, and key witnesses, as well as examine relevant research records and materials. In order to avoid any claims of alteration of data, the Inquiry Committee will promptly attempt to locate and secure the originals of all relevant research data and/or documents if it is ascertained that such data and/or documents may be part of the case. Supervised access to the data and/or documents should be available to the Respondent. The Inquiry Committee may employ such outside resources (e.g., legal or consulting services) as it deems appropriate to assist in the Inquiry. Witness interviews should be summarized in writing, and witnesses given the opportunity to review and correct such summaries of their own statements.

All Inquiries shall be completed within 60 days of initiation unless circumstances clearly warrant a longer period. If circumstances do so warrant, the record of the Inquiry shall include documentation of the reasons for exceeding the 60-day period. Notwithstanding the above, the Inquiry Committee should not feel compelled to use the entire 60-day period if, using fair and appropriately comprehensive methods, they can come to a conclusion more quickly about whether a more substantial Investigation is required.

The individuals selected to conduct the Inquiry shall make every effort to be objective, impartial, and fair. The proceedings of the Inquiry will be kept confidential and will not be disclosed except as necessary to facilitate a complete and comprehensive Investigation.

The Inquiry Committee will evaluate the evidence and testimony obtained during the Inquiry. Upon conclusion of the Inquiry, the Inquiry Committee shall prepare a written report that identifies the evidence reviewed, summarizes relevant interviews, and states the conclusions of the Inquiry. An Investigation is warranted if there is: (1) a reasonable basis for concluding the Allegation falls within the definition of Research Misconduct; and (2) preliminary information-gathering and fact-finding from the Inquiry indicate that the Allegation may have substance. The report must include sufficiently detailed information documenting the Inquiry Committee's recommendation as to whether further Investigation is warranted. The Respondent shall be provided with a copy of the Inquiry Committee's report and shall have ten days to comment on it. The Complainant may be notified and may be provided with relevant portions of the Inquiry Committee's report for comment, which shall be received by the Inquiry Committee within ten days. Any comments made by the Respondent or Complainant will become part of the final report of the Inquiry Committee. Based on the comments, the Inquiry Committee may revise the report as appropriate.

Within 30 days of completing the Inquiry, and after consultation with the Research Integrity Officer and Lifespan's Office of General Counsel, the Inquiry Committee shall transmit the final report to the Deciding Official, who shall determine whether to initiate an Investigation based on the initial findings and whether any interim administrative action is appropriate. In either case, the Deciding Official will notify the Research Integrity Officer, who will then notify the Respondent of the determination and provide Respondent with a copy of the final Inquiry report. The Research Integrity Officer may, in his or her sole discretion, notify the Complainant of the determination and provide the Complainant with relevant portions of the final report. Any previously notified Department Chair, Division Chief, and/or Laboratory Director shall also be informed of the result of the Inquiry. If it is decided that an Investigation is warranted, the sponsoring agency or entity and ORI, if applicable, shall also be notified. If it is necessary to notify ORI, such notification must be done in writing before the date the Investigation begins, must include a copy of the final Inquiry report which includes the name and position of the Respondent(s), the general nature of the Allegation, and the PHS application or grant numbers implicated by the Investigation. The Research Integrity Officer may also notify publications to which results of implicated research have been submitted that an Investigation has been initiated.

F. Investigation

If the Inquiry Committee determines that further investigation is necessary, a formal Investigation will be initiated within 30 days of the completion of the Inquiry. The Research Integrity Officer shall, within the 30-day timeframe, select an <u>ad hoc</u> committee (the "Investigation Committee") to hear the formal charges against the Respondent alleged in the previously described Inquiry. The Research Integrity Officer will take steps to ensure that individuals appointed to the Investigation Committee do not have unresolved personal, professional, or financial conflicts of interest with the Respondent, Complainant, or essential witnesses. The Respondent will be informed of the proposed composition of the Investigation Committee and will have the opportunity to raise objection to individual appointees in writing within seven working days. The Research Integrity Officer shall consider the objections prior to appointing the Investigation Committee.

The Investigation Committee shall fully investigate the charges set forth and recommend appropriate action. The Investigation shall focus on the Allegations and shall examine the factual matters of the case. The Investigation Committee shall take steps to obtain custody of relevant research records and evidence not already secured by the Inquiry Committee. The Investigation will normally include review of all documentation relevant to the Allegation, including, but not necessarily limited to, relevant research records, computer files, proposals, manuscripts, publications, correspondence, memoranda, and notes. The Investigation Committee may employ such outside resources (e.g., legal or consulting services) as it deems appropriate to assist in the Investigation. Interviews of the Respondent, Complainant, and witnesses should be tape-recorded or transcribed.

The Investigation Committee's charge is to generate a report that summarizes the procedures used to conduct the Investigation, all of the information considered, its conclusion as to whether there is sufficient evidence to support the Allegation, and any recommended administrative or disciplinary actions to be taken against the Respondent in the event the Allegation is substantiated. It is within the discretion of the Investigation Committee to incorporate by reference any report from the

Inquiry Committee, to the extent that the Investigation Committee is satisfied with any aspect(s) of the Inquiry Committee report as constituting a comprehensive review and resolution of the issues.

All Investigations should be conducted expeditiously and completed within 120 days if possible. This includes conducting the Investigation, preparing the report of findings, making the report available for comment by the Respondent, and submitting the report to ORI, if applicable. If the 120-day deadline cannot be met, the Investigation Committee shall request an extension from the Research Integrity Officer. If applicable, a written request for an extension and an explanation for the delay must be submitted to ORI. This request to ORI shall include an interim report on the progress to date, an estimate for the date of completion of the report, and any other necessary steps. If this request is granted, periodic progress reports may also be requested by ORI. Notwithstanding the above, the Investigation Committee should not feel compelled to use the entire 120-day period if, using fair and appropriately comprehensive methods, they can come to a conclusion more quickly about whether Research Misconduct occurred, and, if so, how serious the Research Misconduct was and who was responsible.

The Investigation Committee is expected to carry its Investigation through to completion and diligently to pursue all significant issues. If, for any reason, the Investigation Committee decides that it is appropriate or necessary to terminate the Investigation, the approval of the Deciding Official is required. If the Deciding Official approves such termination, a report of the planned termination, including the reasons for the termination, shall be made to ORI, if applicable, which may then decide to undertake its own investigation.

When the Investigation Committee reaches a conclusion regarding an Allegation, it shall submit a preliminary report reviewing all information and its conclusion to the Respondent. The preliminary report shall adequately detail the evidence that supports or refutes each Allegation included in the Investigation. Respondent shall also be given a copy of, or supervised access to, the evidence. Respondent will have 30 days to prepare a response to the preliminary report, which shall be considered by the Investigation Committee before the Investigation report is finalized. The Investigation Committee may, in its sole discretion, provide the Complainant with a copy of the preliminary report or relevant portions of the report. If applicable, the Complainant may be given up to 30 days to submit a response to the preliminary report, which the Investigation Committee shall consider in finalizing the Investigation report.

After receiving the Respondent and/or Complainant's comments to the preliminary report, if any, the Investigation Committee shall prepare and maintain a final Investigation report that explains the specific allegations of research misconduct, lists and adequately substantiates its findings, describes the policies and procedures under which the Investigation was conducted, describes how and from whom information was obtained, and recommends the administrative or disciplinary actions to be taken against the Respondent, if any. If applicable, the report shall also describe and document the PHS support, including, for example, grant numbers, grant applications, contracts, and publications listing PHS support. The final report of the Investigation Committee shall be made available to the Respondent, who will be provided a full and fair opportunity to respond in writing to the Investigation Committee within seven working days of receipt of the final report. Such comments, if any, may be made a part of the record of the Investigation. The final report shall also be provided

to Lifespan's Office of General Counsel for review of its legal sufficiency. Comments shall be incorporated as appropriate.

The final Investigation report, the Complainant's and/or Respondent's comments, if any, and the Investigation Committee's recommended administrative or disciplinary actions, if any, shall be provided to the Deciding Official, who will determine based on a preponderance of the evidence whether to accept the final report, its findings, and any recommended administrative or disciplinary actions. If the Deciding Official's determination varies from that of the Investigation Committee's final report, the Deciding Official will explain in detail the basis for rendering a decision different from that of the Investigation Committee. The Deciding Official's determination, together with the Investigation Committee's final report, constitutes the final Investigation report for purposes of ORI review. If applicable, ORI and/or other government authorities (e.g., the federal Office of Human Research Protections and/or state agencies) should be notified of the final outcome of the Investigation, and ORI shall be provided with a copy of the final report. The final Investigation report provided to ORI shall describe any pending or completed administrative and/or disciplinary actions against the Respondent. The Complainant may be provided with those portions of the final report that address his or her role and opinions in the Investigation.

V. CONSEQUENCES OF INVESTIGATION

A. Administrative and/or Disciplinary Actions

If the Deciding Official determines that the alleged Research Misconduct is substantiated by the findings of the Investigation Committee, he or she will decide on the appropriate administrative or disciplinary actions to be taken, if any, after consultation with the Research Integrity Officer and taking into consideration the recommendations of the Investigation Committee. The actions may include, but are not limited to:

- withdrawal or correction of all pending or published abstracts and papers emanating from the research where Research Misconduct was found;
- removal of the responsible person from the particular project, letter of reprimand, special
 monitoring of future work, probation, suspension, salary reduction, or initiation of steps
 leading to possible rank reduction or termination of employment and/or medical staff
 privileges;
- notification to other hospitals and sponsoring agencies with which the individual has been or is affiliated, if there is reason to believe that previous research may be characterized by Research Misconduct; and,
- restitution of funds as appropriate to granting agencies, Lifespan, and/or research subjects.

The Research Integrity Officer shall notify the Respondent in writing of any administrative or disciplinary actions to be taken and shall also meet with the Respondent to discuss the findings and the implementation of any such administrative or disciplinary actions. Any disciplinary action relating to medical staff privileges and/or IRB or other research committee review shall be coordinated with the Department Chair, Division Chief, Laboratory Director, and/or the IRB or other research review committee, as appropriate. If indicated, medical staff discipline will be

pursued through established medical staff disciplinary procedures, but the procedures in this policy are distinct from, and may be taken without recourse to, medical staff disciplinary procedures.

B. Restoration of the Respondent's Reputation

If the Investigation Committee's finding is that no Research Misconduct occurred and the Inquiry or Investigation has resulted in any damage to the Respondent's reputation, Respondent shall meet with the Research Integrity Officer to discuss how the Respondent's record shall be cleared and what reasonable efforts will be taken to restore the Respondent's reputation. Any Lifespan actions to restore the Respondent's reputation must first be approved by the Deciding Official. The implementation of such approved actions will be the responsibility of the Research Integrity Officer. Depending on the particular circumstances, the Research Integrity Officer should consider notifying those individuals aware of or involved in the Inquiry or the Investigation of the final outcome, publicizing the final outcome in forums in which the Allegation was previously publicized, or expunging all reference to the Allegation from the Respondent's personnel file.

VI. OTHER CONSIDERATIONS

A. <u>Termination of Lifespan Employment or Resignation Prior to Completing Inquiry or Investigation</u>

The termination of the Respondent's Lifespan employment or affiliation, by resignation or otherwise, before or after an Allegation has been reported, will not necessarily preclude or terminate the Research Misconduct procedures, due to the possible compelling interests of Lifespan, research colleagues, the IRB or other research review committee, and research subjects in resolving such Allegations.

If the Respondent refuses to participate in the process after resignation or otherwise, the Inquiry and Investigation Committees will use their best efforts to reach a conclusion concerning the Allegations, noting in their reports the Respondent's failure to cooperate and its effect on the Committee's review of all the evidence.

B. Allegations Not Made in Good Faith

If relevant, the Deciding Official will determine whether the Complainant's Allegations were made in good faith. If an Allegation was not made in good faith, the Deciding Official will determine whether any administrative, employment and/or medical staff action should be recommended against the Complainant. Use of this process for malicious motives or for personal enrichment or aggrandizement shall be dealt with firmly.

VII. RECORD RETENTION

After completion of a case and all ensuing related actions, the Research Integrity Officer will prepare a complete file, including the records of any Inquiry and/or Investigation, copies of all documents and other materials furnished to the Research Integrity Officer or the Committees, and a

complete record of any appeal. The Research Integrity Officer will keep the file in a secure manner for seven years after completion of the case to permit later assessment of the case. ORI or other authorized government personnel will be given access to the records as required by law.

VIII. CONCLUSION

The integrity of a hospital and its medical staff should never be in question. Thus, Lifespan and the medical and scientific community within it must do everything possible to prevent research fraud, unethical treatment of human subjects, or other Research Misconduct in science and research. This policy is meant to vindicate those interests.

IX. Procedure:

If a Lifespan Employee or a Lifespan Professional Staff member has a question concerning the interpretation or applicability to a particular circumstance of any of the laws or regulations referred to in this Policy, such Lifespan Employee or Lifespan Professional Staff member should first consult with his/her supervisor(s) and if his/her supervisor(s) is unable to answer the question or provide any guidance or, if, because of the circumstances, it would be inappropriate to discuss the matter with his/her supervisor(s), then such Lifespan Employee or Lifespan Professional Staff member should contact the Lifespan Senior Vice President/Chief Quality Officer; in any case, the Lifespan Employee or Lifespan Professional Staff member may contact the Office of the General Counsel or the Corporate Compliance Officer for advice. If any Lifespan Employee or Lifespan Professional Staff member is aware of any violation or threatened or potential violation of this Policy, or suspects a violation of this Policy has occurred, such Lifespan Employee or Professional Staff member must refer to the Policy on Code of Conduct for instruction as to what action to take. No adverse action will be taken against any party who reports, in good faith, any violation or apparent or threatened violation.

Exhibit 9

PAGES 1-189

VOI. T

EXHIBITS See Index

UNITED STATES DISTRICT COURT FOR THE DISTRICT OF RHODE ISLAND C.A. NO. 17-cv-00265-M-PAS

DR. DAMIAN MEDICI,

Plaintiff,

vs

LIFESPAN CORPORATION,
RHODE ISLAND HOSPITAL, and
MICHAEL SUSIENKA,

Defendants.

30(b)(6) DEPOSITION of LIFESPAN
CORPORATION AND RHODE ISLAND HOSPITAL, by its
designee, JOHN B. MURPHY, M.D., a witness
called on behalf of the plaintiff, taken
pursuant to the applicable provisions of the
Federal Rules of Civil Procedure, before
Marie C. Leonard, Registered Professional
Reporter, Certified Shorthand Reporter
No. 146799, and a Notary Public in and for the
Commonwealth of Massachusetts, at the offices
of Nixon Peabody, One Citizens Plaza,
Providence, Rhode Island, on Thursday, March 1,
2018, commencing at 10:09 a.m.

KACZYNSKI REPORTING
72 CHANDLER STREET
BOSTON, MA 02116
617.426.6060

KACZYNSKI REPORTING

- 1 Q. Okay. And what's your current position?
- 2 A. Executive vice president for physician affairs
- 3 at Lifespan.
- 4 Q. And how long have you held that position for?
- 5 A. Since 2012.
- 6 Q. And what was your previous position at Rhode
- 7 Island Hospital?
- 8 A. Chief medical officer.
- 9 Q. And how long did you hold that position?
- 10 A. 2008 through 2012.
- 11 Q. And what was your position at Rhode Island
- 12 Hospital prior to that position?
- 13 A. I was the director of graduate medical
- education, and I held that position from 2004
- 15 to 2008.
- 16 Q. Okay. And I may have forgotten. When did you
- 17 go to Rhode Island Hospital, in 2004?
- 18 A. Yeah.
- 19 Q. Okay. Just briefly tell me your educational
- 20 background beginning with college.
- 21 A. Yes. I went to Union College. It's in
- 22 Schenectady, New York. I majored in
- psychology and graduated with a bachelor's in
- science.

1		lecture.
2	Q.	Okay. Are you the deciding official under
3		Lifespan's Research Misconduct Policy?
4	Α.	I am.
5	Q.	And how long have you held that position?
6	Α.	Since 19 I mean, since 2012 when I moved
7		into the role of executive vice president for
8		physician affairs.
9	Q.	Okay. Is it your understanding that if you're
10		the executive vice president of physician
11		affairs, you are also the deciding official?
12	Α.	That was the decision was made in 2012 when
13		this position was created.
14	Q.	Okay. Are you let me let me just ask
15		you
16		MR. HARRINGTON: If I could mark these
17		as exits.
18		Oh, let me I think we should start
19		off with No. 57.
20		(Discussion off the record)
21		(Exhibit No. 57, Notice of Rule 30(b)(6)
22		Deposition of Defendant Lifespan
23		Corporation marked for identification)
24		(Exhibit No. 58, Notice of Rule 30(b)(6)

- 1 investigation committee to find research 2 misconduct with respect to three of the four allegations; is that a fair statement? 3 4 Α. Yes. 5 Okay. And you say that you received the final Ο. 6 report on Monday, August 31; do you see that? 7 Α. Correct. 8 If you'd turn to Exhibit 85, that's Q. 9 August 30th. So does that indicate that 10 probably some -- it was either August 30th or August 31st; is that a fair statement? 11 12 This is dated August 30th, and this is dated Α.
- 14 Q. No, I know. But the 9/3 email says you

August -- that is dated 9/3.

- received -- it was hand-delivered on August 31?
- 16 A. Yes.

13

- 17 Q. Okay. So it was either August 30th or
- 18 August 31 it was hand-delivered to you?
- 19 A. Yes.
- 20 Q. Okay. And then the following day you received
- a response, okay; and then devoted 20 hours to
- 22 review the documents; is that a fair statement?
- 23 A. Not quite. Because it wasn't after I received
- this -- the document on the -- the day after

- that I started reviewing documents. I started
- 2 reviewing them as soon as I received the first
- one.
- 4 Q. Okay. And that was either on the 30th --
- 5 A. And over the course -- over the course of the
- 6 next couple of days I spent 20 hours, yes.
- 7 Q. Okay. From August 30th or 31st until
- 8 September 3rd, you spent 20 hours reviewing?
- 9 A. Yes.
- 10 Q. Okay. Did you review -- what did you review?
- 11 A. I reviewed the full report from the
- investigation committee. I reviewed the
- preliminary response and the final response.
- 14 Q. And during this --
- 15 A. And during that time I also read the
- 16 communication from outside counsel that you
- showed me a couple of minutes ago.
- 18 Q. Okay. And during that time period, after --
- 19 you know, from the time you received the final
- 20 report, did you have any communication with
- 21 Dr. Snyder?
- 22 A. I don't believe so. I may have. But I was
- 23 pretty hunkered down doing it.
- 24 Q. Had you indicated to him that you were going

Exhibit 10

EXPERT REPORT OF SHEILA R. GARRITY, JD, MPH, MBA

I have been retained by counsel for Lifespan Corporation ("Lifespan"), Rhode Island Hospital ("RIH") and Michael Susienka to provide an expert opinion regarding the investigation conducted by Lifespan into allegations of research misconduct by Damian Medici, Ph.D.

I have a J.D. from the University of Maryland, and a Masters of Public Health and an M.B.A. from Johns Hopkins University ("Johns Hopkins"). I have worked in academia for over 30 years in various capacities including as the Managing Editor for the *Annals of Neurology* and as the Director of the Division Research Integrity at Johns Hopkins School of Medicine. In that capacity, I was responsible for insuring that allegations of misconduct were reviewed in accordance with institutional policy along with applicable regulations. While at Johns Hopkins, I received over 100 allegations of misconduct; many were under the jurisdiction of the Office of Research Integrity ("ORI") and several involved working with other institutions.

I was at Johns Hopkins in 2005 when the current regulations regarding research misconduct took effect and worked to revise the institutional policy to be in compliance with the regulations. At that time, ORI contracted with the long-time Research Integrity Officer ("RIO") at Michigan State University, David Wright, Ph.D., to develop a training program for institutional staff tasked with handling allegations of research misconduct involving Public Health Service ("PHS")-funded research. Dr. Wright developed what became known as a "RIO Boot Camp," a two and a half day training designed for RIOs and their institutional Generals Counsel ("GCs"). Johns Hopkins hosted the second RIO Boot Camp in 2007. I was one of the faculty for that Boot Camp and have served at a teaching RIO at several since then. These training programs are well attended and work to address the many differences that exist among institutions handling allegations of research misconduct, and work to harmonize those practices with federal regulations.

I worked with ORI on the production of two training videos relating to research misconduct, *The Lab* and *The Clinic*. I facilitated discussions among faculty, postdocs, graduate students and the scriptwriters. I was part of the RIO focus group that reviewed the films before they were broadly distributed. These two videos are widely used in the responsible conduct of research training worldwide.

I worked with ORI to host the "ORI at 20" conference in Baltimore in 2013. This conference discussed the origins of ORI, which was formed from the merger of the NIH Office of Scientific Integrity and the HHS Office of Scientific Integrity Review. The conference included presentations about the evolution of the ORI and how it became a partner with the research community to help improve the quality of research as well as the public trust in research.

Building on the enthusiasm generated by that conference, a group of RIOs came together to establish the Association of Research Integrity Officers (ARIO). ARIO was formed to bring together institutional RIOs and their GCs to develop best practices for the handling of allegations of research misconduct and to broaden our network. I am the Founding President of ARIO. The first ARIO meeting was hosted by Johns Hopkins in 2013. ARIO's sixth annual meeting will

take place in September 2018 at Case Western Reserve University. ARIO invites our federal partners (staff from the ORI, NSF, OHRP, etc.) to present on best practices and common issues in the handling of research misconduct allegations at the first day of the conference. The remaining day and a half of the meeting is closed to allow institutional RIOs and GCs to speak freely without the presence of federal reviewers or the press.

Currently, I serve as the Associate Vice President for Research Integrity and the RIO at George Washington University. The following areas of research compliance report to me: Office of Human Research/Institutional Review Boards; Animal Research Facility/Institutional Animal Care and Use Committee; Office of Laboratory Safety/Institutional Biosafety Committee; Financial Conflicts of Interest; Responsible Conduct of Research; Research Misconduct; and Export Control. I continue to have an excellent relationship with my federal colleagues, have presented at the NSF, and hosted the "Quest for Research Excellence" conference with ORI in the summer of 2017. A copy of my Curriculum Vitae is attached here as Exhibit 1.

I have not testified in the past four years in court or deposition. For my work relating to this expert report, I am being compensated at a rate of \$350/hour.

I have based my opinion on my review of the documents identified in Exhibit 2.

I do not know Damian Medici nor do I know the individuals involved in the research misconduct investigation that is the subject of this report.

I. SUMMARY OF LIFESPAN'S RESEARCH MISCONDUCT INVESTIGATION

A. Background

As of approximately August 2012, Dr. Medici was employed as a Research Associate/Research Scientist in the Department of Orthopaedics at RIH and an Associate Professor at Brown University's School of Medicine. Dr. Medici was the recipient of at least two PHS-funded grants, the funding from which flowed through RIH to Dr. Medici's lab.

In March 2014, Michael Susienka, a medical student at Brown University Medical School brought concerns regarding potentially duplicated and manipulated images in certain of Dr. Medici's publications and proposed publications to Dr. Elizabeth Harrington, Associate Dean for Graduate and Postdoctoral Education at the Medical School. Specifically, Mr. Susienka alleged that images appearing in several articles on which Dr. Medici was a co-author (and in several cases the corresponding author) were duplicates of images appearing in other publications on which Dr. Medici was a co-author. Mr. Susienka made similar allegations with respect to a manuscript co-authored by Dr. Medici and Dr. Logan Walsh, among others (the "Walsh Manuscript"). The Walsh Manuscript had been submitted for publication to a number of scientific journals while Dr. Medici was employed by RIH. The sets of duplicate images purported to represent the results of different experiments conducted under different conditions. After discussions with Dr. Harrington, Mr. Susienka, accompanied by Dr. Harrington, brought his allegations to Dr. Peter Snyder, Lifespan's Chief Research Officer and RIO.

While Dr. Snyder was assessing the allegations, Mr. Susienka came forward with additional allegations regarding Dr. Medici's potential manipulation of experiments then being conducted in Dr. Medici's lab. Two other individuals working in Dr. Medici's lab, Diana Ramirez and Melissa Ramirez, joined in making those allegations. In accordance with Lifespan's policy, Dr. Snyder completed an assessment and determined that the allegations were sufficiently specific and credible to warrant an inquiry.

Dr. Snyder appointed a four-member inquiry committee (the "Inquiry Committee") and submitted Mr. Susienka's allegations to that committee for consideration. The Inquiry Committee issued its report and recommendations in May 2014, concluding that there was sufficient evidence to move forward to investigation. On May 20, 2014, Dr. John Murphy, Lifespan's Deciding Official (DO), accepted the Inquiry Committee's recommendations and asked for the initiation of an investigation into the allegations. Because PHS-funded grants supported the research under question, the decision to initiate an investigation and a copy of the Inquiry Report with Dr. Medici's response were transmitted to the ORI.

Dr. Snyder appointed and convened a four-member investigation committee (the "Investigation Committee"), which met on numerous occasions from June 2014 through April 2015. The Investigation Committee, in consultation with the ORI and Harvard Medical School's RIO, determined that certain of the allegations brought forward by Mr. Susienka should be referred to Harvard Medical School and Harvard Dental School ("Harvard"), where Dr. Medici had been employed when the articles at issue in those allegations were published. Accordingly, Lifespan referred those allegations to Harvard to investigate pursuant to its own policies and procedures.

The Investigation Committee issued its preliminary report on May 20, 2015. The report concluded that Dr. Medici had engaged in research misconduct with respect to three of four allegations it reviewed. The preliminary report was provided to Dr. Medici for his comments. The final report was issued on August 18, 2015, and was also provided to Dr. Medici for comment.

The Investigation Committee's final report, along with Dr. Medici's preliminary and final responses, was submitted to Dr. Murphy, on August 30, 2015. Dr. Murphy considered these materials and decided to adopt the findings of the Investigation Committee, On September 4, 2015, Lifespan submitted the Investigation Committee's final report, along with Dr. Medici's comments thereto, to the ORI as required. The ORI acknowledged receipt of the report, but, as of the date of this Report, has taken no further action.

While Lifespan's investigation was proceeding, Harvard was simultaneously reviewing the allegations that had been referred. Harvard referred to an inquiry committee allegations regarding eight sets of duplicated images in articles co-authored by Dr. Medici. In October 2016, Harvard issued the report of its Inquiry Committee reviewing the referred allegations. The report concluded that there was sufficient evidence of research misconduct to warrant further investigation. Based upon documents produced by Dr. Medici in this litigation, Harvard has not issued the report of its Investigation Committee.

B. Summary of Opinions Expressed in this Report

Lifespan conducted a thorough, competent, objective and fair investigation into the allegations of research misconduct relating to Dr. Medici. The Inquiry and Investigation Committees charged with reviewing the misconduct allegations were staffed with experienced scientists with no prior relationship with Dr. Medici and with the expertise necessary to consider the allegations and preside over the investigation. Both Committees interviewed the essential witnesses, sequestered and reviewed relevant documents and other evidence and supported their conclusions through careful reasoning and citation to evidence.

Moreover, Dr. Medici was provided with sufficient due process to respond to the allegations. Dr. Medici was notified of the inquiry and investigation proceedings and the specific allegations. He was provided with access to the evidence that Lifespan collected relating to the investigation and he had more than ample opportunity to gather any additional evidence he deemed relevant. The responses and information provided by Dr. Medici were considered by both the Inquiry and Investigation Committees and by the DO, who had the ultimate responsibility to determine whether an investigation was merited and whether the Investigation Committee's findings should be adopted.

I have reviewed the Expert Report of Dr. Alan R. Price and believe his conclusions are based on a selective review of the documents relating to the process and a less than objective view of those documents and the processes typically undertaken by institutions in reviewing allegations of research misconduct. It is my opinion that there were no material breaches of the Lifespan Policy and/or regulations, as suggested by Dr. Price, and that, even if we assume for argument's sake that certain breaches did occur, they did not affect the thoroughness or fairness of the process, Dr. Medici's ability to respond to the allegations, or the outcome of the investigation.

II. DEFINITION OF RESEARCH MISCONDUCT

Under the applicable regulations, research misconduct is defined as "fabrication, falsification, or plagiarism in proposing, performing or reviewing research, or in reporting research results." Significantly for purposes of the Lifespan investigation, research misconduct involving the reporting of research results is not limited to instances in which such reports are contained in published articles. Any form of reporting results, including the reporting of results in lectures, abstracts, posters, or papers presented at conferences or even presented internally within the researcher's institution, can give rise to research misconduct. Indeed, PHS-funded institutions, which are required to take steps to foster research integrity (see 93 C.F.R. § 302(a)(2)), are obligated to address potential research misconduct *before* the results of such misconduct makes its way into the published record.

In addition, research misconduct is not limited to instances in which other scientists or the public are actually misled or harmed by the misconduct that has occurred. Dr. Medici has asserted that he is in possession of images from the research reported in the Walsh Manuscript and that those images are so similar to images that were inadvertently included in the Walsh Manuscript that no one could have been misled by the Walsh Manuscript had it been published as originally submitted. Without opining on whether others could or could not have been misled

by the inclusion of the erroneous images, the inclusion of those images justifies a finding of misconduct if the preponderance of the evidence shows it was done intentionally, knowingly or recklessly, and if using images from another experiment to represent the results of a different experiment qualifies as a significant departure from accepted practices of the relevant research community. The proper storing of research data is a basic tenant of the responsible conduct of research. In preparing a manuscript for publication or in reviewing the work of one's mentees, it is expected that the primary data will be examined and a clear path from the work done at the bench to the results presented should be traceable.

III. SIGNIFICANCE OF RESEARCH MISCONDUCT

Science is largely a field of collaboration. Researchers build off the results of other researchers. The experimental results generated by one group of scientists become the foundation upon which another group of scientists builds. It is this collaboration that propels science forward. This collaboration cannot work without trust. The scientific community has neither the time nor the resources to replicate all scientific results, and so scientists must trust that the data and results generated and reported by others are reported honestly and are accurate.

Research misconduct in science erodes that trust, and in doing so has a significant impact on researchers and the public and private entities that fund them, on the institutions that employ researchers and support their work, on the larger scientific community and on the public. Where misconduct occurs in scientific research, the funds that supported that research are wasted, further work based on that research must be questioned and perhaps replicated, and the public has cause to question the critical role of research. Indeed, research misconduct in science can cause medical doctors to pursue incorrect treatments, which can change standard treatment protocols and can have a direct impact on patients.

Research misconduct also has a profound impact on the institutions at which that misconduct occurs. Institutions rely on external funding to pay for many of the costs associated with conducting research. That funding not only allows the institution to employ research scientists and to purchase equipment. It also funds the training of students, the employment of technicians, statisticians, administrative staff, and facility support. In addition, institutions are ranked by the amount of funding (especially federal funding) that they are awarded. These rankings allow institutions to attract faculty, students, and other funding. A finding of misconduct could have a devastating impact on an institution. Graduate students may be displaced. The institution's reputation may be harmed, impairing its ability to attract students, faculty, and funding. It can lead to the termination of a number of employees.

For all of the above reasons, institutions are justifiably focused on preventing, detecting and addressing research misconduct. Institutions take allegations of research misconduct seriously not simply because federal regulations require them to do so, but because of the significant impact research misconduct may have on the institutions themselves.

IV. PURPOSE OF RESEARCH MISCONDUCT REGULATIONS AND THE ROLE OF ORI

Regulations issued by the Department of Health and Human Services regarding research misconduct, appearing at 42 C.F.R. Part 93, took effect in June 2005 (the "Regulations"). The Regulations are understood to be a response to what was seen at that time as a growing trend of high profile research misconduct cases, including those involving the University of Alabama at Birmingham and the University of Vermont. These cases involved fabricated and/or falsified data used to apply for federal research grants.

The Regulations place initial responsibility for insuring the integrity of PHS-funded research on the institutions that receive those finds. To that end, the Regulations charge institutions with adopting policies for addressing claims of research misconduct and also charge institutions with creating an environment that fosters the responsible conduct of research.

Some criticized the Regulations for moving scientific disputes into the legal arena. That criticism was countered by highlighting the government's role in protecting public funds. Under the Regulations, institutions that receive allegations of research misconduct are required to respond to those allegations promptly. An institution's failure to adequately address allegations that fall within the scope of the Regulations can have serious repercussions for the institution. Institutions that fail to adequately address allegations of research misconduct can be found in violation of their institutional assurances and are at risk of losing their ability to apply for federal funding.

The ORI plays a specific role with respect to allegations of research misconduct, but that role is different than the role played by institutions. As noted above, institutions have a range of interests they may be seeking to protect through their policies concerning research misconduct and their investigations of research misconduct allegations. The ORI has different interests.

One of the ORI's roles is to insure institutional compliance with the Regulations. The ORI will often direct institutions to provide copies of their policies for ORI review. However, as acknowledged by the Regulations (see 93 C.F.R. 102(c)), the specific provisions of Part 93 operate as a floor rather than as a ceiling. Institutions are free to adopt different policies and procedures, including policies that define research misconduct more broadly than do the Regulations or create another category of "professional" misconduct, as long as the minimum requirements are met.

When an institution makes a determination, upon completion of an inquiry, that an investigation is warranted, it must transmit that decision to the ORI, along with a copy of the inquiry report. The ORI reviews the inquiry report making certain the allegations are framed with specificity so that an institutional investigation may be conducted. At this point the ORI typically assigns a Division of Investigative Oversight (DIO) number to the case. It is my understanding that the DIO number is also entered into a PHS database which allows PHS funding agencies to know if one of the grants a particular agency funded is involved in a research misconduct review process. The Regulations give institutions 120 days to complete an investigation. In my experience, investigations are rarely completed in 120 days and the ORI regularly grants extensions for completion of an investigation.

Once an investigation is complete, the results must be transmitted to the ORI with a copy of the investigation report. The ORI reviews the institution's report, at which point it may "determine if the institution conducted the proceedings in a timely and fair manner," "conduct additional analyses and develop evidence," and "decide whether research misconduct occurred," among other actions. The ORI may also choose to take no action at all.

The standards applied by the ORI in deciding whether to make a finding of research misconduct following an institutional finding are not addressed in the Regulations. In my experience, the ORI makes a finding of research misconduct in only a small percentage of cases submitted that contain institutional findings of research misconduct. The decision by the ORI to take no action in response to an institutional finding of research misconduct does not reflect the ORI's views of the merits of that particular institutional finding. In my professional career, I have submitted approximately 20 findings of research misconduct to the ORI. The ORI has taken no action with respect to any of those cases, neither making findings of research misconduct nor determinations with respect to whether processes that led to those findings were timely and fair.

V. OVERVIEW OF RESEARCH MISCONDUCT INVESTIGATIONS

As discussed above, where research misconduct allegations arise at a PHS-funded institution, the institution is generally responsible for investigating the alleged misconduct in the first instance. Under the Regulations, a two-stage process is used to address the allegations. Many institutions employ a RIO and a DO to guide the process. While the RIO, DO and the individuals conducting the review of allegations of research misconduct are guided by the Regulations and internal policies, many aspects of the process are within the discretion of the RIO, DO and investigation committees. Such discretion is essential given the varying kinds of research misconduct that can occur and varying ways in which it can occur.

A. The Research Integrity Officer and Deciding Official

Many institutions, including Lifespan, employ a RIO and a DO to address research misconduct allegations. The roles of the RIO and DO are not defined by the Regulations, although most institutional policies contain mention of both positions. Generally, the RIO is the recipient of the allegations of research misconduct and is tasked with overseeing the institution's procedures involving review of allegations. RIOs typically have substantial responsibilities with respect to the handling of research misconduct investigations. They also have substantial discretion with respect to aspects of the process. For example, RIOs have substantial discretion regarding (i) when to share transcripts and other evidence with the respondent, being mindful of the risks to complainants and others when evidence is shared with the respondent; (ii) who to inform about the investigation and how much to tell them; and (iii) when to notify journals or others regarding the allegations.

RIOs work closely with their institutions' offices of general counsel. General counsels help insure that the interests of the institution are protected. Respondents are increasingly represented by outside counsel, essentially requiring the participation of counsel on behalf of the institution. Where litigation is threatened, as occurred at the outset of Lifespan's investigation

into research misconduct by Dr. Medici, legal advice is all but required to insure that institution, as well as the members of the inquiry and investigation committees, are protected from unnecessary legal exposure.

The DO is responsible for making the determination as to whether to accept the recommendation of the inquiry committee and the findings of the investigation committee. DOs typically work closely with the RIO, will stay abreast of the progress of the inquiry and any investigation, and may weigh in on aspects of the inquiry and investigation processes and related actions, for example with respect to employment status or other actions that may be taken with respect to a complainant or respondent.

B. The Two-Stage Process

The Regulations provide that allegations of research misconduct are to be addressed using a two-stage process. Before this process commences, the institution (usually via the RIO) must determine whether the first stage — the inquiry — is warranted. An inquiry is warranted when the allegation of research misconduct falls within the definition of research misconduct and is sufficiently credible and specific so that the potential research misconduct may be identified. At this point, the institution and the RIO are not conducting any evaluation of the merits of the allegation or the motive of the Complainant. If the allegations are specific enough to articulate alleged misconduct, an inquiry should be commenced.²

Assuming an inquiry is warranted, the institution commences the two-stage process set forth in the Regulations. The purpose of the inquiry is to determine if the allegations may have substance, or to determine if there is a "there there." The inquiry is a preliminary process. Only an "initial review" of the evidence is required. Witnesses are typically interviewed and records are typically reviewed. additional witnesses and documents are almost always identified at the investigation stage. The purpose of an investigation is to determine whether an investigation is warranted.

An investigation is warranted if the allegation "may have substance." Frivolous, unjustified, or mistaken allegations do not merit an investigation, nor do allegations that do not actually allege research misconduct (for example, an allegation that is determined to be solely an authorship dispute or argument over intellectual property rights presented in the guise of research misconduct); substantive and specific allegations do. Significantly for purposes of this investigation, claims of honest error by the respondent are not to be addressed at the inquiry stage, but at the investigation stage, where the respondent has the burden of establishing that the alleged misconduct is the subject of honest error.³

¹ May 16, 2014 email from D. Medici to P. Snyder (LIFESPAN-4801-02).

² Examples of allegations that would not meet this standard include anonymous allegations that do not identify who is allegedly perpetrating the misconduct or what the misconduct is and allegations that suggest that the respondent is "falsifying data" without specifying what data or the manner in which it is being falsified.

³ See 70 Fed. Reg. at 28378 (stating that given the preliminary nature of the fact finding at the inquiry stage, "it would be appropriate for the inquiry report to note if there is possible evidence of honest error or

The inquiry committee (assuming the inquiry is conducted by committee, which is not required), must issue a report of its findings and recommendations. The inquiry committee's report, along with the respondent's comments, are typically provided to the DO, who makes the ultimate determination as to whether to proceed to investigation. If the DO decides an investigation is warranted, that decision, along with the report and respondent's comments, are provided to ORI. This is the first report to the ORI regarding the alleged misconduct.

The notice and procedural requirements that apply at the inquiry stage are minimal in part because of the low evidentiary bar that applies. The inquiry committee (or other individual such as the RIO if a committee process is not used) is not tasked with determining the actual merit of an allegation, and thus the role of the Respondent in "defending" against allegations at the inquiry stage is minimal. The Respondent is entitled to written notice of the inquiry and an opportunity to comment on the inquiry report.

The bulk of the investigative work in the review of research misconduct allegations is typically conducted at the investigation stage. The investigation committee is specifically charged with taking "reasonable steps to insure an impartial and unbiased investigation," and to insure that the investigation is thorough and sufficient documented. Interviews are to be recorded or transcribed and additional research records are to be collected and sequestered.

The investigation committee is also specifically charged with pursuing "significant issues and leads discovered that are determined to be relevant to the investigation, including any evidence of additional instances of possible research misconduct." Because of this, it is extremely common for the scope of the investigation to differ from the scope of the inquiry and for the scope of the investigation to shift as the investigation proceeds. Often, the allegations referred by the inquiry committee result in being only a subset of the allegations ultimately investigated by the investigation committee. In addition, given the significantly different scope of the investigations conducted at the inquiry and investigation stages, it is common for issues not addressed at the inquiry stage to be addressed at the investigation stage.

The investigation committee must determine if the alleged misconduct occurred and if so, who is responsible. It must also determine if the misconduct was knowing, intentional, or reckless and whether it was a deviation from the expected standards of the particular field of study. The evidentiary burden is also higher at the investigation stage. The standard of review is preponderance of the evidence, i.e. more likely than not. The institution has the burden of proof for making a finding of research misconduct based on the evidence gathered. However, the respondent's failure to provide research records is evidence of research misconduct where respondent had the opportunity to maintain the records and did not do so. Nothing bars the

difference of opinion for consideration in the investigation, but it would be inappropriate for the inquiry

disproving possible honest error or differences of opinion") (emphasis added).

report to conclude, on the basis of an initial review of the evidence of honest error or difference of opinion, that the allegation should be dismissed. The determination of whether the alleged misconduct is intentional, knowing, or reckless, including consideration of evidence of honest error or difference of opinion, should be made at the investigation stage, following a complete review of the evidence. As noted in the preamble of the OSTP final policy, institutions and HHS do not have the burden of

respondent from coming forward, at any time, with evidence that s/he believes is relevant to the investigation.

VI. OVERVIEW OF THE LIFESPAN INQUIRY AND INVESTIGATION

Based on my experience and my review of the documents relevant to Lifespan's investigation into allegations of research misconduct involving Dr. Medici, I believe Lifespan's investigation was thorough, competent, objective and fair and complied with the Regulations and all material provisions of the Lifespan Policy.

A. The Lifespan Policy

Lifespan adopted a policy on research misconduct as required by the Regulations (the "Lifespan Policy"). The Lifespan Policy is similar to other institutional policies and contains the required elements. Lifespan has submitted a copy of its policy to the ORI as part of the required annual assurance.

The Lifespan Policy provides a clear description of how allegations of research misconduct will be reviewed. It describes the different roles of the RIO and the DO, as well as the rights afforded to the complainant, the respondent, the witnesses and others involved in the process. The Lifespan Policy clarifies certain aspects of the investigation process not specifically addressed by the Regulations. For example, the Lifespan Policy provides that the inquiry and investigation be conducted by committees, whereas the Regulations whereas the Regulations do not specify how the inquiry and investigation be conducted and would permit various types of proceedings, including review by a single individual. The Lifespan policy also describes the process for submission of the inquiry and investigation reports to the DO, a process not described in the Regulations.

B. "Jurisdiction"

Neither the Regulations nor the Lifespan Policy contain any provisions regarding the circumstances in which a particular institution has "jurisdiction" over a particular allegation of research misconduct. In fact, the concept of "jurisdiction" is all but absent from research misconduct proceedings; the applicability of the regulations — and the requirements that flow from them — is premised on whether an institution receives PHS funding in connection with the research about which an allegation has been made. The applicability creates affirmative obligations but does not conversely delineate matters into which an institution is *forbidden* from wading. Typically, research misconduct investigations will take place at the institution where the alleged misconduct occurred, although it is not unusual for allegations to span several institutions when an investigator has moved between institutions. Determining the best approach to a multi-jurisdictional investigation is not addressed by the Regulations and is usually a case-by-case assessment — often with the ORI's input — as to the best approach for a given matter.

At the time Mr. Susienka came forward with allegations of research misconduct, Dr. Medici was an employee of RIH, one of the Lifespan-member hospitals. Two of the allegations involved the Walsh Manuscript, which Dr. Medici had submitted while at RIH. Indeed, Dr.

Medici listed his affiliation with RIH when he submitted the manuscript.⁴ Based on these factors alone, Lifespan had an obligation to consider the allegations. Moreover, before the inquiry process began, Mr. Susienka (together with Diana and Melissa Ramirez) came forward with an additional allegation regarding on-going activities in Dr. Medici's lab. This allegation obviously fell squarely within Lifespan's purview.

During the course of the inquiry, Dr. Medici stated that the research underlying the Walsh Manuscript was conducted while at Harvard. However, this fact does not relieve Lifespan of its duty or right to conduct the investigation at issue. The evidence indicates that Dr. Medici prepared the Walsh Manuscript while at RIH. Because the allegation was that Dr. Medici had falsified that manuscript by including images from a different article (representing different research), and not that research underlying the Walsh Manuscript was falsified, the misconduct being investigated in fact occurred at RIH. Nor was it improper for Lifespan to look into the allegations regarding duplicated images in articles submitted while Dr. Medici was at Harvard. In my experience, the ORI generally prefers that allegations of research misconduct brought against an individual be investigated at a single institution, even if that misconduct occurred at more than one institution. That is especially true where the allegations are related or arise out of the same sort of misconduct, as was the case with Dr. Medici.

Significantly, at no time did the ORI take the position that Lifespan did not have proper "jurisdiction" over the investigation. Indeed, while Lifespan later referred the allegations relating to the articles published while Medici was at Harvard to Harvard, the decision to do so was not in response to an instruction from the ORI. The ORI's only recommendation relevant to jurisdiction was that Lifespan "may consider contacting the Research Integrity Officer (RIO) at the prior institution if additional data is needed that is not at Lifespan..." Lifespan contacted Harvard to discuss the allegations just two weeks later. It was through correspondence with Harvard and consultation with the ORI that the allocation of the allegations to be investigated was determined. ORI was advised of the final allocation and made no objections.

Lifespan continued to consult with the ORI throughout the course of its investigation as is customary and as, it can be assumed, Harvard did as well. At no time was Lifespan instructed that it should refer the allegations it was investigating to Harvard or that it did not have the authority to investigate those allegations; nor did ORI ever question the fact that Lifespan inquired into the entire scope of allegations prior to the negotiated apportionment with Harvard.

⁴ September 18, 2014 email from C. Struss to T. Eckford (LIFESPAN-2462-88).

⁵ May 30, 2014 letter from S. Garfinkel to P. Snyder (LIFESPAN-12603-06).

⁶ June 13, 2014 email from P. Snyder to G. Brodnicki (LIFESPAN-6831-32).

⁷ September 18, 2014 letter from K. Heffernan to G. Brodnicki (LIFESPAN-1301-02); September 1, 2015 Letter from K. Heffernan to J. Murphy (LIFESPAN-1301-2)

C. Inquiry

Mr. Susienka brought forward specific and credible allegations of potential research misconduct by Dr. Medici. The allegations were specific as they identified seven specific instances of potential image duplication in manuscripts and articles authored by Dr. Medici and illustrated the alleged duplications in a clear manner. The allegations fell within the definition of research misconduct because they involved potential falsification of research records.

Dr. Snyder, in his capacity as the RIO, prepared a charge for the Inquiry Committee that summarized the allegations brought forth by Mr. Susienka. The charge informed the Inquiry Committee of the purpose of the inquiry, which was to make a preliminary evaluation of the evidence and testimony, and not to determine whether research misconduct occurred. Moreover, the members of the Inquiry Committee were provided with Lifespan's Policy to insure that they understood and complied with the Policy's requirements.

Dr. Medici was provided with oral notice of the inquiry on April 9, 2014, ¹⁰ and received written notice of the inquiry on April 11, 2014. ¹¹ The April 11, 2014 notice also apprised Dr. Medici of the members of the Inquiry Committee and attached a copy of the Lifespan Policy, which outlined the inquiry and investigation processes. In contrast with the notice required at the Investigation stage, neither the Regulations nor the Lifespan Policy require Lifespan to advise Dr. Medici of the specific allegations being evaluated by the Inquiry Committee. Nonetheless, Dr. Medici was provided with the evidence of the potential duplicate images identified by Mr. Susienka on April 21, 2014. ¹²

The Inquiry Committee interviewed relevant witnesses, including Dr. Medici, Mr. Susienka, Diana Ramirez and Melissa Ramirez, and other individuals who worked in Dr. Medici's lab. The Inquiry Committee also reviewed the images that were the subject of Mr. Susienka's allegations. After concluding that the seven sets of images identified by Mr. Susienka indeed appeared to be duplicates, the Inquiry Committee concluded that an investigation was warranted. The Inquiry Committee prepared a written report consistent with the Regulations and the Lifespan Policy. Dr. Medici was provided with a copy of the Inquiry

⁸ April 1, 2014 memo from P. Snyder (DM 904-06); March 31, 2014 email from M. Susienka to P. Snyder (LIFESPAN-10579-88)

⁹ Relying on notes of Dr. Snyder's charging of the Inquiry Committee — notes most likely prepared by Dr. Snyder's assistant — Dr. Price concludes that Dr. Snyder instructed the Inquiry Committee to make a recommendation for a "full panel (hearing)" and that Dr. Snyder expected that Dr. Medici would be the subject of sanctions, including dismissal and being barred from federal funds." This is an obvious misreading of the notes of the charging meeting. Indeed, Dr. Snyder and Dr. Saab, who were actually in the room at the time, made clear that the instruction was that the Inquiry Committee was to determine whether or not an investigation, i.e. a full panel hearing, was warranted. The reference to the potential sanctions, which of course the Inquiry Committee had no ability to impose, was intended to advise the Committee of the seriousness of the endeavor.

¹⁰ April 9, 2014 memo from P. Snyder (LIFESPAN-14223).

¹¹ April 11, 2014 email from C. Saab to D. Medici (LIFESPAN-93-94).

¹² April 21, 2014 email from C. Saab to D. Medici (LIFESPAN-568-87).

Committee's Report on May 6, 2014^{13} and, consistent with the Lifespan Policy, was provided with ten days to comment upon it.

Dr. Medici made two submissions to the Inquiry Committee. On April 25, 2014, in response to questions posed by the Inquiry Committee at his interview and before the Inquiry Committee finalized its report, Dr. Medici emailed a letter directly to the members of the Inquiry Committee. There is every reason to believe that each member of the Inquiry Committee received and considered the letter, although only the Chair of the Inquiry Committee, Dr. Carl Saab, was asked to confirm in writing that he reviewed it. On May 16, 2014, Medici submitted his formal response to the Inquiry Committee. The response was received and reviewed by the members of the Inquiry Committee, each of whom confirmed that nothing in Dr. Medici's response caused them to change their recommendation that the matter proceed to investigation.

Having received and considered Dr. Medici's response to their report, having determined that such response did not change the recommendations of the Inquiry Committee and having finalized its report, the Inquiry Committee's work concluded. Based on my years of participation in research misconduct proceedings, it is my strong opinion that the evidence before the Inquiry Committee was well beyond what was needed to merit an investigation. Moreover, it is my opinion that Dr. Medici was given sufficient notice, opportunity to comment and to otherwise provide information or exculpatory evidence throughout the inquiry process.

D. Decision to Proceed to Investigation

Upon receiving the Inquiry Committee's report and Dr. Medici's response, Dr. Snyder forwarded the documents to Dr. Murphy, the DO. 18 Although not required to do so, Dr. Snyder also included Dr. Medici's April 25, 2014 letter to the Inquiry Committee. 19 Dr. Snyder also asked Dr. Jack Wands, a colleague with substantial experience reviewing western blots and micrographs, to conduct a blinded review of the images that were alleged to be duplicates. Dr. Wands agreed with the Inquiry Committee's conclusion that the images in question were indeed duplicates. 20

¹³ May 6, 2014 letter from P. Snyder to D. Medici (LIFESPAN-16123-24).

¹⁴ April 25, 2014 email from D. Medici to C. Saab (LIFESPAN-157-63).

¹⁵ May 19, 2014 email from C. Saab to P. Snyder (LIFESPAN-2962-63); April 6, 2018 Dep. of C. Saab at pp. 144-45 and 175-76.

¹⁶ May 16, 2014 letter from D. Medici (LIFESPAN-4807-17).

¹⁷ May 21, 2014 email from A. Ayala to P. Snyder (LIFESPAN-95-96); May 21, 2014 email from P. Snyder to C. Saab (LIFESPAN-208-09); May 21, 2014 email from V. Knopik to M. Carey (LIFESPAN-164-65).

¹⁸ May 19, 2014 email from P. Snyder to J. Murphy (LIFESPAN-612).

¹⁹ May 20, 2014 email from J. Murphy to P. Snyder (LIFESPAN-6969-70).

²⁰ May 20, 2014 email from P. Snyder to J. Murphy (LIFESPAN-4287).

Dr. Murphy received and reviewed the documents in question and decided to adopt the Inquiry Committee's recommendation that the matter proceed to an investigation. Dr. Murphy communicated that decision to Dr. Snyder on May 20, 2014.²¹

Dr. Price points to various emails and other correspondence from Dr. Snyder to argue that Dr. Snyder decided to proceed to an investigation before the Inquiry Committee completed its work and before Dr. Murphy considered whether to adopt the Inquiry Committee's recommendation. While Dr. Snyder's written correspondence is admittedly imprecise, the evidence indicates that it was the Inquiry Committee, and not Dr. Snyder, that interviewed witnesses, considered evidence and made the determination as to whether an investigation was warranted, and that it was Dr. Murphy who reviewed that determination, along with Dr. Medici's response, and made the ultimate decision to proceed to an investigation. Moreover, while Dr. Snyder took certain steps to prepare for the investigation prior to receiving Dr. Murphy's decision, the Investigation Committee was not convened and did not begin its work until after Dr. Murphy decided that the investigation should proceed.

E. The Investigation

Dr. Snyder selected four experienced scientists to serve on the Investigation Committee. Dr. Medici was notified of the proposed Committee members on May 23, 2014.²² Dr. Medici objected to the selection of Dr. Ulrike Mende as one of the Committee members, claiming that Dr. Mende had received confidential information from Dr. Snyder regarding Dr. Medici.²³ Although Lifespan believed that there was no evidence to indicate that Dr. Mende's receipt of the information would affect her ability to serve on the Investigation Committee, Lifespan agreed to replace Dr. Mende with Dr. Adam Chodobski. Dr. Medici was informed of Dr. Chodobski's appointment to the Investigation Committee on June 16, 2014.²⁴

The Investigation Committee convened on June 25, 2014.²⁵ At that meeting, the Investigation Committee receive its charge and background information relevant to the investigation. The Investigation Committee was also provided with a list of the allegations to be investigated. That same list of allegations was provided to Dr. Medici six days earlier, on June 19, 2014.²⁶

At this point in time, the allegations the Investigation Committee was charged with reviewing included allegations relating to articles that were published while Dr. Medici was employed by Harvard because, as discussed above, the ORI had indicated that Lifespan was

 $^{^{21}}$ May 20, 2014 email from J. Murphy to P. Snyder (LIFESPAN-6969-70); March 1, 2018 Dep. of J. Murphy at p. 172.

²² May 23, 2014 letter from T. Eckford to H. Cooper (LIFESPAN-7479).

²³ June 3, 2014 letter from H. Cooper to T. Eckford (LIFESPAN-723-24).

²⁴ June 16, 2014 letter from T. Eckford to H. Cooper (LIFESPAN-676).

²⁵ June 25, 2014 Meeting Agenda (LIFESPAN-13839).

²⁶ June 19, 2014 letter from K. Heffernan to H. Cooper (LIFESPAN-552-55).

authorized to investigate all of the allegations and Harvard had not yet accepted referral of any of the allegations.

The Investigation Committee promptly began its collection and review of evidence. In addition to Dr. Medici, who was interviewed on October 7, 2014, the Investigation Committee interviewed eight other individuals that either worked in Dr. Medici's lab or collaborated with Dr. Medici. Each of the interviews was transcribed by a licensed court reporter and each witness was provided with a transcript of his or her interview to review and correct.

The Investigation Committee had additional questions for Dr. Medici, many of which related to the allegations involving experiments Dr. Medici conducted in March and April 2014. The Investigation Committee asked Dr. Medici to appear for an additional interview,²⁷ but Dr. Medici declined.²⁸

Dr. Medici was provided supervised access to all of documentary evidence sequestered by Lifespan, and that evidence was reviewed by Dr. Medici and his counsel on December 8, 2014.²⁹ Dr. Medici was asked, on numerous occasions over the course of the investigation, to provide evidence relevant to the images and research at issue. Requests for source data relating to the allegations were made at Dr. Medici's interview before the Inquiry Committee on April 21, 2014,³⁰ and in writing on May 6, 2014,³¹ on May 19, 2014,³² on September 29, 2014,³³ November 12, 2014,³⁴ and December 2, 2014,³⁵ among other occasions. Dr. Medici refused to provide any source data relating to his research. He also declined to return the laptop that was issued to him (and purchased) by Lifespan.³⁶

The only evidence provided by Dr. Medici was eight image files. As an initial matter, the files, which were subsequently produced in this litigation, do not constitute "source data." The images have been cropped and otherwise prepared for publication. For example, with respect to the western blot images that Dr. Medici provided, the full blot showing the primary source of the research results was not provided. The primary or source data would be the results that came from the experimental equipment rather than the image created from the source data to create

²⁷ December 4, 2014 email from P. Shaw to C. Hale (LIFESPAN-6823-25).

²⁸ December 9, 2014 email from C. Hale to K. Heffernan (LIFESPAN-2310-14).

²⁹ December 5, 2014 email from M. Borreliz to H. Cooper (LIFESPAN-2862-64).

³⁰ April 25, 2014 email from D. Medici to C. Saab (LIFESPAN-157-63)

³¹ May 6, 2014 email from P. Snyder to D. Medici (LIFESPAN-2388-89).

³² May 19, 2014 email from P. Snyder to D. Medici (LIFESPAN-3061-62).

³³ September 29, 2014 email from K. Heffernan to C. Hale (LIFESPAN-2730).

³⁴ November 12, 2014 letter form K. Heffernan to C. Hale (LIFESPAN-1799-1801).

³⁵ December 2, 2014 letter from K. Heffernan to C. Hale (DM 1224-25).

³⁶ December 5, 2014 email from M. Borreliz to H. Cooper (LIFESPAN-2862-64).

³⁷ Images files, Medici Dep. Ex. 39.

figures for publication. Some journals now require copies of the source data to insure the integrity of the data represented by figures submitted for publication.

The image files were shown to the members of the Investigation Committee by Dr. Medici during his interview by showing the images in "jpeg" format on his laptop to the Investigation Committee members. Dr. Medici did not provide the image files themselves, which would have allowed the Investigation Committee members to examine the images and their source data in detail. Finally, Dr. Medici was unable to explain the provenance of the files. It remains unclear where the files were located and how it was that Dr. Medici determined that the files related to research that was conducted for the Walsh Manuscript.

The Investigation Committee issued its preliminary report on May 20, 2015.³⁸ The report concluded that there was sufficient evidence to find that Dr. Medici had engaged in research misconduct with respect to three of the four allegations reviewed by the Investigation Committee. The report documented the evidence that had been reviewed and the reasons for the Investigation Committee's conclusions.

Dr. Medici was given 30 days to respond to the preliminary draft report, as provided for by the Lifespan Policy and the Regulations.³⁹ Dr. Medici was subsequently given an additional two weeks to respond in response to his request for an extension.⁴⁰ Dr. Medici's response was received, reviewed, and discussed by the Investigation Committee. Revisions to the preliminary draft report were made to address certain of the points raised by Dr. Medici, but the Investigation Committee affirmed its conclusions with respect to each of the allegations.

The Investigation Committee issued its final report on August 18, 2015. Dr. Medici submitted his response to the final report on August 27, 2015. The Chair of the Investigation Committee forwarded the Investigation Committee's Final Report to the DO, Dr. John Murphy, on August 30, 2015. Dr. Murphy also received Dr. Medici's responses to the Preliminary and Final Reports. Dr. Murphy devoted twenty hours to reviewing the final report and Dr. Medici's response. Dr. Murphy accepted the findings of the Investigation Committee with respect to each of the allegations. (*Id.*)

³⁸ Preliminary Report of the Lifespan Investigation Committee (LIFESPAN-2193-2224).

³⁹ May 20, 2015 letter from K. Heffernan to C. Hale (LIFESPAN-2191-22).

⁴⁰ June 4, 2015 email from K. Heffernan to H. Cooper (LIFESPAN-4471-78).

⁴¹ Both the Final Report and Dr. Medici's response included attached exhibits, including the evidence considered by the Investigation Committee and much of the correspondence relied upon by Dr. Price in his report.

⁴² September 3, 2015 email from J. Murphy to P. Snyder (LIFESPAN-517).

On September 4, 2015, Lifespan submitted the final report and Dr. Medici's response to the ORI.⁴³ The ORI acknowledged receipt but has taken no action with respect to Lifespan's investigation or Dr. Medici's alleged misconduct.⁴⁴

Based on my substantial experience with research misconduct investigations and my review of the evidence in this matter, it is my opinion that the Investigation Committee's investigation was exceedingly thorough. The Investigation Committee reviewed a substantial amount of evidence and documented its conclusions regarding that evidence with an appropriate level of detail. I believe the evidence more than supports the Investigation Committee's conclusions. Moreover, I believe the Investigation Committee complied with its obligations under the Regulations and the Lifespan Policy, including those obligations concerning the fairness and due process afforded to Dr. Medici.

VII. ISSUES RAISED BY ALAN PRICE

I have carefully reviewed the report prepared by Dr. Price. From the face of his report, it appears that Dr. Price reviewed only a selection of the documents reviewed by the committees involved in the research misconduct review at Lifespan and at Harvard. His conclusions are inconsistent with an impartial application of the Regulations and the available evidence.⁴⁵ I will not address each of the issues discussed by Dr. Price, but respond to some of his concerns below.

A. Jurisdiction and Collaboration with Harvard

Dr. Price raises a series of concerns regarding Lifespan's decision to proceed with an inquiry into the allegations of misconduct, Lifespan's contacts with Harvard regarding its inquiry and Lifespan's attempt to obtain evidence that might be in Harvard's possession that could relate to the inquiry and investigation process.

Dr. Price's assertion that Lifespan acted improperly in proceeding with the inquiry instead of alerting Harvard's RIO to the allegations received is inconsistent with my significant experience with research misconduct review processes. As noted above, at least two of the allegations brought forward by the complainant involved a manuscript Dr. Medici submitted for publication while employed by RIH. Before the Inquiry Committee was convened, the complainant came forward with allegations regarding possible on-going misconduct in Dr. Medici's lab. As such, Lifespan had the right, and indeed the obligation, to proceed with the

⁴⁴ September 11, 2015 email from R. Ambalavanar to M. Borreliz (LIFESPAN-556-57). The ORI has indicated that it will await the result of Harvard's investigation into Dr. Medici's alleged misconduct before taking any action it deems necessary. October 26, 2015 email from P. Snyder to R. Ambalavanar (LIFESPAN-0002583-86).

⁴³ September 4, 2015 letter from J. Murphy to S. Garfinkel (LIFESPAN-6709-12).

⁴⁵ Dr. Price opined that Lifespan's investigation was the "worst administratively handed, most unfair research conduct case that [has has] ever reviewed." The ORI, where Dr. Price was Acting Director of the Division of Investigative Oversight, apparently did not concur. After receiving and review Lifespan's Investigation Report and Dr. Medici's response, which addressed many if not all of the issues addressed in Dr. Price's report, the ORI stated that it "did not find any major concerns." October 26, 2015 email from P. Snyder to R. Ambalavanar (LIFESPAN-2583-86).

inquiry. In addition, and again as noted above, at no point did the ORI question Lifespan's decision to proceed with an inquiry and then an investigation into the allegations.

At this point, Dr. Snyder determined that the allegations were specific and credible, but needed to convene the Inquiry Committee to determine whether an investigation was warranted in accordance with Lifespan's policy and procedures. Had Dr. Snyder contacted Harvard's RIO prior to making such a determination, and had the Inquiry Committee concluded that the evidence did not merit an investigation, Dr. Medici would almost certainly have complained that Dr. Snyder breached his confidentiality obligations.

After Lifespan completed the inquiry and submitted its report to the ORI, the ORI responded that Lifespan "may consider contacting the Research Integrity Officer (RIO) at the prior institution if additional data is needed that is not at Lifespan. . . " The ORI did not instruct Lifespan to refer any or all of the allegations to Harvard, despite its power to do so. Pursuant to 42 C.F.R. § 402, when the ORI becomes aware of an allegation of research misconduct, as it did when Lifespan reported the results of its inquiry, it may "conduct an initial assessment or refer the matter to the relevant institution for an assessment, inquiry, or other appropriate actions." The ORI could have referred the investigation to Harvard. It did not. Indeed, the ORI never suggested that Lifespan's review or any or all of the allegations was improper and it was directly involved in discussions between Harvard and Lifespan regarding the eventual allocation of the allegations. At no time did the ORI object to the agreed-upon division of responsibility.

Dr. Price further suggests that it was improper for Investigation Committee to consider, in the course of its review, the alleged duplicated images that were the subject of Harvard's review. The Investigation Committee would have been remiss had it failed to review additional instances of image duplication when considering Dr. Medici's "honest error" defense. In most cases, investigation committees are required to make credibility determinations and evidence of an additional seven instances of image duplication was directly relevant to the credibility determinations the Lifespan Investigation Committee was required to make.

Dr. Price suggests that Lifespan delayed discussing the allegations with Harvard's RIO and requesting data from Harvard. This is simply not the case. Less than two weeks after the ORI suggested that Lifespan "may consider contacting" the Harvard RIO, Peter Snyder had a detailed discussion with Gretchen Brodnicki, Harvard Medical School's RIO. Following that conversation, on June 13, 2014, Dr. Snyder sent Ms. Brodnicki an email with attached documents relevant to the allegations and the inquiry conducted by Lifespan. In that email, Dr. Snyder requested that Harvard provide "all potentially retrievable source records related to the published studies in question, as well as any source images (digital or film) be retrieved and sequestered for use in our investigation." Unfortunately, Harvard was unable to locate the requested records, and thus provided no such documents to Lifespan. 47

⁴⁶ June 13, 2014 email from P. Snyder to G. Brodnicki (LIFESPAN-6831-32).

⁴⁷ Dr. Price cites an August 12, 2014 email from Ms. Brodnicki in which she expresses concerns regarding the Lifespan inquiry as evidence of Lifespan's failure to properly consider its jurisdiction with respect to the allegations. August 12, 2014 email from G. Brodnicki to K. Heffernan (LIFESPAN-4254-56). Dr. Price conveniently fails to cite Ms. Brodnicki's subsequent communication on this matter in

Over the following months, Lifespan and Harvard continued to communicate regularly regarding the allocation of the allegations between the institutions. In September 2014, Harvard agreed that Lifespan should refer the allegations relating to the articles that had been published while Dr. Medici was at Harvard. On September 18, 2014, Lifespan formally referred those allegations to Harvard, ⁴⁸ and in November 2014, forwarded additional information that came to light regarding Dr. Medici's earlier publications. ⁴⁹

Harvard immediately undertook its review of the allegations referred by Lifespan. Although Ms. Brodnicki had originally expressed concern regarding the inquiry conducted by Lifespan into the allegations that were subsequently referred to Harvard, Harvard apparently later determined that its concerns were unfounded because it decided that it could proceed straight to the investigations stage based on the inquiry that Lifespan had conducted.⁵⁰ It was only when Dr. Medici complained that doing so would be improper that Harvard decided to conduct its own inquiry into the allegations.⁵¹ Harvard's Inquiry Committee issued its report on October 26, 2016.⁵² The report concluded that there was sufficient basis to proceed to an investigation with respect to each of the allegations.

A. Notice of Inquiry and Allegations to Medici

Dr. Price opines that Lifespan's inquiry and investigation were flawed because Dr. Medici was not provided with notice of the formal allegations in a timely manner. The Regulations provide that the respondent be notified of the inquiry in writing "at the time of or before" the inquiry begins. The Lifespan Policy also provides for notice to the respondent, but does not specify whether such notice must be in writing. Neither the Regulations nor the Lifespan Policy state that the respondent must receive notice of the "formal allegations" at this time, in contrast to the Regulations relating to the investigation stage, which do require notice of formal allegations.

which, after being provided with additional information by Lifespan's counsel regarding the inquiry conducted by Lifespan, she states "our conversation helped me tremendously to understand the steps RIH took at inquiry, and gain more confidence in the possibility to HMS's proceeding on Allegations 1-4 at investigation." August 13, 2014 email from G. Brodnicki to K. Heffernan (LIFESPAN-4274-79).

⁴⁸ September 18, 2014 letter from K. Heffernan to G. Brodnicki (LIFESPAN-1301-02). The fact that Ms. Brodnicki, who has served as a Director of Research Integrity for 17 years and has unquestionably overseen a substantial number of research misconduct investigations apparently concluded that Lifespan, and not Harvard, should retain "jurisdiction" over the allegations relating to the Walsh Manuscript despite the fact that the research for that manuscript was conducted at Harvard further undermines Dr. Price's conclusion that all of the allegations should have been referred to Harvard at the outset.

⁴⁹ November 6, 2014 email from K. Heffernan to G. Brodnicki (LIFESPAN-2678-82).

⁵⁰ September 22, 2014 letter from G. Brodnicki to D. Medici (produced by defendant without a Bates number).

⁵¹ February 11, 2015 letter from C. Hale to G. Brodnicki (produced by defendant without a Bates number).

⁵² October 26, 2016 Report of Inquiry Panel (produced by defendant without a Bates number).

Dr. Medici was notified verbally of the inquiry on April 9, 2014, and in writing on April 11, 2014.⁵³ The Inquiry Committee was charged on April 8, 2014 and interviewed its first witnesses on April 11, 2014.⁵⁴ Whether Dr. Medici was notified of the inquiry before the inquiry "began" is arguable, given that neither the Regulations or the Lifespan Policy specify whether the inquiry begins upon charging or upon beginning its work.

In any event, Dr. Medici received written notice of the inquiry ten days before he was interviewed which, in view of the timeline in which the full inquiry process is to be completed, was ample time for Dr. Medici to prepare himself for his interview and to take any other steps he deemed necessary. Dr. Medici was provided with an opportunity to provide any and all information he deemed relevant both after his interview and within the timeframe provided for him to respond to the Inquiry Report. There is simply no reason to believe that the minor delay in providing written notice had any impact on the outcome of the Inquiry or on Dr. Medici's ability to defend himself during the inquiry process.

Dr. Medici's formal notice of the allegations was entirely consistent with the Regulations and the Lifespan Policy. Dr. Medici was provided with written notice of the allegations on June 19, 2014, before the Investigation Committee was convened. The allegations were modified on two occasions, once to provide further specificity and once to reflect the referral of four of the allegations to Harvard. Dr. Medici was provided with written notice in both instances. No additional notices regarding the allegations were required or are typical in research misconduct investigations.

B. Transcript of Inquiry Committee Interview

Dr. Price makes much of the fact that Dr. Medici was not provided with a transcript of his interview before the Inquiry Committee. The Lifespan Policy provides that interviews before the Inquiry Committee are to be summarized in writing. The Regulations contain no provision regarding the recording of interviews before the Inquiry Committee. The available evidence indicates that all witness interviews were recorded, but that an issue with the recording device rendered the recordings difficult to decipher. Members of the Inquiry Committee attempted to create a transcript, but it appears that the quality of the recording was so poor that the transcript's accuracy could not be confirmed. Accordingly, Dr. Medici was not provided with a transcript of his interview during the inquiry process. It is important to note that the Inquiry Committee also did not receive transcripts of the recorded interviews.

While Lifespan's failure to provide Dr. Medici with a summary of his interview constitutes a deviation from the Lifespan Policy, there is no evidence whatsoever that this deviation impacted the outcome of the inquiry or Dr. Medici's ability to defend himself during the inquiry process. First, it is important to keep in mind the low evidentiary bar that applies at the inquiry stage. The evidence presented at the inquiry stage overwhelmingly established that the allegations "may have substance," and Dr. Medici's access to a summary of his interview would not have changed that fact. Second, Dr. Medici apparently had sufficient recall of the

⁵³ April 9, 2014 memo from P. Snyder (LIFESPAN-14223); April 11, 2014 email from M. Medici to C. Saab (LIFESPAN-93-94).

⁵⁴ Lifespan Inquiry Committee Summary Report (LIFESPAN-257-263)

subject of his interview to provide the Inquiry Committee with a three-page letter addressing the subject of his interview, which he did on April 25, 2014.⁵⁵ Third, Dr. Medici was provided with the recording of his interview on August 11, 2014, almost two months before Dr. Medici was interviewed by the Investigation Committee.⁵⁶ Dr. Medici had ample opportunity to raise any issues arising from his review of the recording during his interview with the Investigation Committee, or at any time before or after his interview. Dr. Medici never raised any issues arising from his review of the recording.

Most significantly, the purpose of a policy providing for the summarizing of inquiry committee interviews (and permitting the interviewees the opportunity to review them for accuracy) is to insure that the record before the Investigation Committee is accurate. The primary purpose of the summary is not to assist the inquiry committee which, after all, was present for the interview itself. Here, the Investigation Committee was also without the benefit of the interview summaries. Thus, Dr. Medici and the Investigation Committee were on equal footing in that regard.

It is my opinion that Lifespan's failure to provide Dr. Medici with a summary or recording of his interview before the Inquiry Committee had no impact on the thoroughness or fairness of the Inquiry process.

C. Sequestration and Access to Files

Dr. Price raises a series of unfounded issues relating to Lifespan's sequestration of documents and data relating to the investigation and Dr. Medici's access to the files that Lifespan sequestered.

First, Dr. Price alleges that Lifespan failed to request research records from Harvard in a timely manner. As noted above, Lifespan requested those files immediately following the conclusion of the inquiry and upon the ORI's suggestion that Lifespan could coordinate with Harvard with respect to its allegations. While Lifespan theoretically could have reached out to Harvard earlier, Lifespan also had to consider its confidentiality obligations and Dr. Medici's reputation in deciding whether and when to contact his prior institution.

The Inquiry Committee had no obligation to review the research records relating to the publications at issue in order to complete the preliminary evaluation that occurs at the inquiry stage. The allegation before the Inquiry Committee involved the duplication of images in articles and manuscripts, not the validity of the research associated with those published articles and manuscripts.

Second, Dr. Price mistakenly asserts that Lifespan did not seek research records or other evidence from Dr. Medici in a timely manner. Indeed, Dr. Price suggests that Lifespan did not make such a request of Dr. Medici until November 2014. The documents I reviewed suggest otherwise. On numerous occasions, Lifespan requested that Dr. Medici produce source data and other evidence relevant to the allegations. As referenced in Dr. Price's report, Dr. Snyder

⁵⁵ April 25, 2014 email from D. Medici to C. Saab (LIFESPAN-157-63).

⁵⁶ August 11, 2014 letter form K. Heffernan to C. Hale (DM 1170).

requested that Dr. Medici provide any materials in his possession that were relevant to the allegations on May 6, 2014.⁵⁷ On May 19, 2014, Dr. Snyder requested that Dr. Medici indicate whether he had the source files, i.e. the research records for the images in question. Dr. Medici failed to respond. Lifespan made an additional request for source data on September 29, 2014. On November 12, 2014, Lifespan requested that Dr. Medici to return laptop computers in his possession, at least one of which had been purchased by and was the property of Lifespan. Dr. Medici did not provide any data in response to these requests nor did he return the laptop computers. Moreover, regardless of the numerous requests by Lifespan for relevant research records, nothing prevented Dr. Medici from coming forward, at any time, with relevant records.

I believe that Dr. Price also errs in placing responsibility for the absence of relevant research data on Lifespan. As the senior and corresponding author on the Walsh manuscript, Dr. Medici had the responsibility to maintain the research records relating to that manuscript. His inability to come forward with any such research records except, miraculously, images of unknown origin that correspond to the alleged duplicated images was rightfully considered by the Lifespan Investigation Committee. This is so specifically in light of 93 C.F.R. § 93.106, which provides that the absence of or the respondent's failure to provide research records adequately documenting the questioned research as evidence of research misconduct where the respondent "had the opportunity to maintain the records and did not do so."

Finally, Dr. Price opines that Dr. Medici was not provided with sufficient access to the records that Lifespan did sequester. As an initial matter, this position is curious given that Dr. Medici has long argued that none of the relevant records existed at Lifespan, thus suggesting that his need to review the records in Lifespan's possession was minimal at best. In any event, Dr. Medici was given full and timely access to the sequestered documents. The Regulations do not provide an absolute right for the respondent to have access to sequestered records, either at the inquiry or investigation stage. The Lifespan Policy, with which Dr. Medici was provided at the outset of the inquiry, provides that supervised access should be "available" to the respondent at the inquiry stage and, at the investigation stage, the respondent should be provided with "supervised access" to the evidence upon completion of the preliminary report.

Dr. Medici's first request for access to sequestered data was made through his counsel, on August 6, 2014.⁵⁸ Counsel for Lifespan responded the next day, agreeing to provide Dr. Medici's counsel with access to the sequestered records before Dr. Medici's interview by the Investigation Committee. Dr. Medici and his counsel ignored the offer until October 3, 2014, just days before Dr. Medici's scheduled interview. At that time, Dr. Medici's counsel demanded that Lifespan produce copies of all the sequestered material, which Dr. Medici was not entitled to

⁵⁷ Dr. Price indicates that this request was improper because it sought Dr. Medici's assistance in obtaining records from Harvard. There was nothing improper about this request. Dr. Medici performed the research in question and would be in the best position to locate the records. Lifespan made its own, similar request to Harvard, but that fact does not absolve Dr. Medici from any responsibility for locating the records relating to research that he was attempting to publish. Indeed, simply by submitting the Walsh manuscript for publication, Dr. Medici was representing that he had access to the underlying research records. If he had no access to those records, he was in breach of his obligations to the journals with whom he was hoping to publish.

⁵⁸ August 7, 2014 email from K. Heffernan to C. Hale (DM 1167).

receive.⁵⁹ On October 6, 2014, Lifespan's counsel reiterated that Dr. Medici could have supervised access to the data, and made this offer again on November 12.⁶⁰ It was not until December 8, 2014 that Dr. Medici made arrangements to avail himself of Lifespan's offer of supervised access to the records that had been offered four months earlier. Significantly, Dr. Medici's counsel reviewed the sequestered records over five months before the Investigation Committee's preliminary report was issued (the time at which Dr. Medici was entitled to access to the evidence under the Lifespan Policy).

Based on my substantial experience with research misconduct investigations, Dr. Medici was provided with more than sufficient opportunity to review the evidence collected by Lifespan. Moreover, he had ample time after his review of the evidence to prepare his response to the Preliminary Report or, if he deemed necessary, to provide an interim assessment of the evidence and the allegations. Lifespan's approach to the sequestration of evidence and Dr. Medici's access thereto is entirely consistent with, if not more generous than, that of many institutions in research misconduct investigations.

D. Confidentiality

Dr. Price opines that Lifespan breached its confidentiality obligations in a number of ways. I disagree with this opinion. In fact, based on my experience, Lifespan took substantial steps, more than are required by the Regulations, to preserve the confidentiality of the proceedings.

Both the Regulations and the Lifespan Policy generally require that Lifespan treat research misconduct allegations and proceedings confidentiality, the confidentiality obligations are not absolute. Indeed, the Regulations provide only that ""[d]isclosure of the *identity of respondents and complainants* in research misconduct proceedings is limited, to the extent possible, to those who need to know, consistent with a thorough, competent, objective and fair research misconduct proceeding, and as allowed by law." 42 CFR § 93.108(a) (emphasis added). The Regulations say nothing about the obligation to maintain confidentiality as to other aspects of the proceedings beyond the identity of the individuals implicated.

Moreover, the confidentiality obligation applies only "to the extent possible." The Regulations recognize that some information sharing is critical to conducting a thorough, competent, objective and fair proceeding and it is within the institution's discretion to determine how to balance those obligations appropriately. The Lifespan Policy contains substantially identical language, in addition to a general requirement that "[t]he rights and reputation of all

⁵⁹ October 3, 2014 letter from C. Hale to K. Heffernan (DM 1201-04).

⁶⁰ October 6, 2014 letter from K. Heffernan to C. Hale (DM 1205-06); November 12, 2014 letter from K. Heffernan to C. Hale (DM 1214-16).

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parties involved ... must be protected throughout these procedures." Policy at III(B). Moreover, the Regulations and the Lifespan Policy specifically provide for disclosure to the Complainant, including allowing the Complainant to review and comment on the inquiry report (42 C.F.R. § 93.308(b)) and the investigation report (42 C.F.R. § 93.312(b)).

Dr. Price raises concerns regarding a series of communications with Mr. Susienka (the original complainant), Diana Ramirez and Melissa Ramirez, both of whom worked in Medici's lab and who subsequently came forward with allegations of research misconduct against Dr. Medici. These communications did not breach the Regulations or Lifespan Policy because Mr. Susienka and Diana and Melissa Ramirez already knew the identity of the respondent. Indeed, as co-complainants, they were entitled to receive the information communicated, which was the result of the inquiry. The fact that neither communication contained a "confidential" header is beside the point as there is absolutely no evidence that Mr. Susienka, Diana Ramirez or Melissa Ramirez shared information about the investigation beyond each other, each of whom was entitled to the information they had.

Dr. Price spills much ink discussing Dr. Snyder's communications with granting agencies in which he informed those agencies of the existence and (in certain cases) the status of the investigation into potential research misconduct by Dr. Medici. Dr. Price appears to be unaware of the fact that the granting agencies may have already known about the investigation because, as noted above, the ORI maintains a database that is available to the granting agencies that notes when a grant is implicated in a research misconduct proceeding. Indeed, it appears from the documents cited by Dr. Price that Dr. Snyder's communications were made in an effort to preserve the grants for Dr. Medici in the event he was found not to have engaged in research misconduct.

Dated: July 13, 2018

Sheila R. Garrity

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Exhibit 1

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3405 Greenway Work: (202) 994-0664 Cell: (443) 838-5049 Unit 204 E-mail: sheila.garrity@gmail.com Baltimore, Maryland 21218

EDUCATION

JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH	Baltimore, MD 21205
Master of Public Health	May 2006

Certificate in Health and Human Rights May 2006

UNIVERSITY OF MARYLAND SCHOOL OF LAW Baltimore, MD 21201

May 2003 Juris Doctor Student Bar Association member 1999 - 2003

Class President 2000-2001, 2002-2003

Class Vice-President 2001-2002

Peer Advisor 2000-2001, 2001-2002 Peer Coordinator 2002-2003

Cunningham Award Recipient – Outstanding Community Service May 2003

THE JOHNS HOPKINS UNIVERSITY School of Professional Studies Baltimore, MD 21218

Master of Business Administration December 1999

THE JOHNS HOPKINS UNIVERSITY School of Professional Studies Baltimore, MD 21218

Master of Science in Business May 1994

CARROLL COLLEGE Helena, MT 59601

Bachelor of Arts in English May 1985

LEGAL EXPERIENCE

UNIVERSITY OF MARYLAND SCHOOL OF LAW

Baltimore, MD 21201 Clinical Law Program 2001-2002

Mediation Program

Completed 80 hours of formal mediation training (certified mediator)

Handled cases referred for mediation by the District Court of Baltimore City

Attended District Court on weekly basis seeking cases to mediate

EMPLOYMENT

GEORGE WASHINGTON UNIVERSITY

Office of Vice President for Research

Washington, DC 20052

Home: (410) 243-1556

Associate Vice President for Research Integrity

January 2015 - Present

Executive Director, Research Integrity and Compliance

June 2014 – December 2014

Oversees the Office of Human Research; Office of Laboratory and Radiation Safety; Animal Research Facility; and Regulatory Affairs and Outreach

Advises the Vice President for Research, senior leadership, faculty, and staff on matters related to research compliance and research ethics

Serves as the University's Research Integrity Officer

Serves as authorized Institutional Official for the Human Research Protections Program, Animal Welfare Program, and Laboratory Safety Program

Provides operational leadership and/or guidance for research processes associated with Federal Funding Accountability and Transparency Act reporting, Freedom of Information Act requests, Export Controls, Financial Conflict of Interest, research document retention and destruction,

management of compliance-related data, and other research related processes

Develops policies, training resources, guidance materials, and processes regarding research integrity and compliance matters

Keeps abreast of federal and state regulation and compliance requirements

Represents the Vice President for Research and the unit at internal/external meetings to advise on matters related to research integrity and compliance

JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE

Office of Policy Coordination Director, Division of Research Integrity

Baltimore, MD 21201 May 2007 – May 2014

Managed inquiries and investigations into allegations of misconduct

Mediated authorship and data ownership disputes

Advised senior leadership, faculty and staff on responding to misconduct allegations

Staffed the Standing Committee on Discipline

Provided training and education in the responsible conduct of research; served as a core faculty member in the IRB-required REWards course (research ethics workshops about duties and responsibilities of scientists)

Served as guest lecturer at other schools both within the University and at other institutions on the topics of research misconduct and the responsible conduct of research

Developed and implemented policies related to research integrity and the responsible conduct of research

Advised other divisions within the University on issues involving misconduct

Served as a consultant to the Office of Research Integrity (ORI)

Served as core faculty for the ORI's Research Integrity Officer Bootcamps

Assistant Director August 2005 – May 2007

Developed and implemented policy in areas of conflict of interest,

conflict of commitment, misconduct, research integrity, board of

director service, and use of the institution's name

Staffed inquiries and investigations into cases of research and professional misconduct in accordance with federal and institutional regulations

ANNALS OF NEUROLOGY

Baltimore, MD 21218 May 1997 – January 2006

Managing Editor

Responsible for entire operations of editorial office

Developed annual budget

Supervised all editorial and clerical staff

Coordinated activities with publisher, Editor-in-Chief, Editorial Board, and sponsoring society

MEMBERSHIPS Council of Science Editors 1997 - 2006 **Society for Scholarly Publishing** 1999 - 2006 **Maryland Bar Association, Member** 2006 - Present **National Association of College and University Attorneys** 2006 - Present Association of Research Integrity Officers (ARIO), Founding Member 2013 - Present Report on Research Compliance, Editorial Advisory Board Member 2014 – Present Public Responsibility in Medicine and Research (PRIM&R), Member 2014 – Present Council on Government Relations (COGR), Member 2014 - Present

Exhibit 2

Materials Considered by Sheila Garrity, JD, MPH, MBA

<u>Date</u>	Bates Start	Bates End	Description
10/15/2012	LIFESPAN-0000279	LIFESPAN-0000291	Lifespan Policy on Research Misconduct (Snyder Dep. Exh. No. 1)
3/31/2014	LIFESPAN-0010579	LIFESPAN-10588	Email from M. Susienka to P. Snyder re: Files
4/1/2014	DM-000904	DM-000906	P. Snyder Memo regarding Meeting with M. Susienka on 5/31/2014
4/2/2014 4/2/2014	LIFESPAN-0001111 DM-000907	LIFESPAN-000115 DM-000909	Email string between M. Susienka and P. Snyder re: Confidential Update - and a request Notes of Michael Susienka
4/2/2014	DIVI 000307	DIVI 000303	Notes of Michael Susicina
4/2/2014	LIFESPAN-0010412	LIFESPAN-0010414	Email from P. Snyder to M. Susienka
4/4/2014	LIFESPAN-0001119	LIFESPAN-0001121	Email from Y. Tseng to P. Snyder
4/7/2014	LIFESPAN-0001122		Email from M. Susineka to P. Snyder
4/8/2014 4/8/2014 4/9/2014	LIFESPAN-15060 LIFESPAN-0009044 LIFESPAN-0014223		Email from P. Snyder to C. Saab Minutes from First Meeting of the Lifespan Inquiry Committee P. Snyder Memo to File re: Meeting with D. Medici
4/11/2014	LIFESPAN-0000093	LIFESPAN-0000094	Email string between D. Medici and C. Saab re: Request for Interview
4/17/2014 4/21/2014	LIFESPAN-0015054 LIFESPAN-0000568	LIFESPAN-0000587	Email from C. Saab to P. Snyder Email from C. Saab to D. Medici re: Follow Up Material
4/25/2014	LIFESPAN-0000157	LIFESPAN-0000163	Email from D. Medici to Inquiry Committee attaching follow up letter
4/28/2014 5/2/2014 5/5/2014 5/5/2014	LIFESPAN-0000257 DM-000982 LIFESPAN-0000308 LIFESAPN-00104033	LIFESPAN-0000263 LIFESAPN-00104035	Lifespan Inquiry Committee Summary Report Email from P. Snyder to D. Medici Email from P. Snyder to D. Ramirez, M. Ramirez and M. Susienka Email from P. Snyder to M. Susienka
5/6/2014	LIFESPAN-0016123	LIFESPAN-0016124	Letter from P. Snyder to D. Medici enclosing copy of report of the Inquiry Committee

Materials Considered by Sheila Garrity, JD, MPH, MBA

<u>Date</u>	Bates Start	Bates End	Description
5/6/2014	LIFESPAN-0002388	LIFESPAN-0002389	Email from P. Snyder to D. Medici re: Preparation for Interview by Investigative Committee
5/16/2014 5/16/2014 5/16/2014	LIFESPAN-0004807 LIFESPAN-0004801 DM-001044	LIFESPAN-0004817 LIFESPAN-0004802	Additional follow up letter from D. Medici to Inquiry Committee Email from D. Medici to P. Snyder Memo from P. Snyder
5/19/2014	LIFESPAN-0002962	LIFESPAN-0002963	Email from C. Saab to P. Snyder confirming receipt of Medici follow up letter after Inquiry Committee meeting
5/19/2014	LIFESPAN-0000612		Email from P. Snyder to J. Murphy with original Inquiry Committee Report and responses from Dr. Medici
5/19/2014	LIFESPAN-0003061	LIFESPAN-0003062	Email from P. Snyder to D. Medici re: Request for archival source images
5/20/2014	LIFESPAN-0004287		Email from P. Snyder to J. Murphy, T. Eckford and K. Arnold re: Res. Misconduct Case
5/20/2014	LIFESPAN-0006969	LIFESPAN-0006970	Email from J. Murphy to P. Snyder, T. Eckford and K. Arnold re: Res. Misconduct Case
5/21/2014	LIFESPAN-0000095	LIFESPAN-0000096	Email from A. Ayala to P. Snyder and Inquiry Committee confirming support of initial decision by Inquiry Committee
5/21/2014	LIFESPAN-0000208	LIFESPAN-0000209	Email from C. Saab to P. Snyder and Inquiry Committee confirming support of initial decision by Inquiry Committee
5/21/2014	LIFESPAN-0000164	LIFESPAN-0000165	Email from V. Knopik to P. Snyder and Inquiry Committee confirming support of initial decision by Inquiry Committee
5/22/2014	LIFESPAN-0000817	LIFESPAN-0000820	Letter from P. Snyder to S. Garfinkel re: Initiation of Research Misconduct Investigation at Rhode Island Hospital
5/22/2014	DM-001093	DM-001095	Letter from T. Eckford to H. Cooper
5/23/2014	LIFESPAN-0007479		Letter from T. Eckford to H. Cooper re: potential Investigation Committee Members
5/30/2014	LIFESPAN-0012603	LIFESPAN-0012606	Letter from S. Garfinkel to P. Snyder
6/3/2014	LIFESPAN-0000723	LIFESPAN-0000724	Letter from H. Cooper to T. Eckford re: Medici review of candidates for Investigation Committee
6/12/2014	LIFESPAN-0008017		Email from P. Snyder to S. Garfinkel

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Materials Considered by Sheila Garrity, JD, MPH, MBA

Email from P. Snyder to G. Brodnicki re: Research Misconduct Investigation Involving H.M.S. LIFESPAN-000676 6/19/2014 LIFESPAN-0000552 LIFESPAN-0000555 Letter from K. Heffernan to H. Cooper re: allegations 6/24/2014 LIFESPAN-0015578 LIFESPAN-0015579 Email from R. Amabalavanar to P. Snyder 6/25/2014 LIFESPAN-001198 7/8/2014 LIFESPAN-0001198 1/8/2014 LIFESPAN-0001198 1/8/2014 LIFESPAN-0000482 LIFESPAN-0000494 8/7/2014 DM-001167 DM-001169 Email from P. Snyder to G. Brodnicki re: Research Misconduct Investigation Involving H.M.S. Letter from T. Eckford to H. Cooper re: response to 6/3/2014 letter regarding potential Investigation Committee members Letter from K. Heffernan to H. Cooper re: allegations Email from R. Amabalavanar to P. Snyder Agenda for Meeting of Investigation Committee and Charge to Committee Femail from Y. Oh to P. Snyder Email from Y. Oh to P. Snyder Email from C. Saab to C. Saab Email string between K. Heffernan and C. Hale enclosing recording of Medici's	<u>Date</u>	Bates Start	Bates End	<u>Description</u>
regarding potential Investigation Committee members 6/19/2014 LIFESPAN-0000552 LIFESPAN-0000555 Letter from K. Heffernan to H. Cooper re: allegations 6/24/2014 LIFESPAN-0015578 LIFESPAN-0015579 Email from R. Amabalavanar to P. Snyder 6/25/2014 LIFESPAN-0013839 7/8/2014 LIFESPAN-0001198 LIFESPAN-0001200 Email from Y. Oh to P. Snyder 7/31/2014 LIFESPAN-0000482 LIFESPAN-0000494 Email from C. Saab to C. Saab 8/7/2014 DM-001167 DM-001169 Email string between K. Heffernan and C. Hale	6/13/2014)14 LIFESPAN-0006831	LIFESPAN-0006832	Investigation Involving H.M.S.
6/24/2014 LIFESPAN-0015578 LIFESPAN-0015579 Email from R. Amabalavanar to P. Snyder Agenda for Meeting of Investigation Committee and Charge to Committee 7/8/2014 LIFESPAN-0001198 LIFESPAN-0001200 Email from Y. Oh to P. Snyder 7/31/2014 LIFESPAN-0000482 LIFESPAN-0000494 Email from C. Saab to C. Saab 8/7/2014 DM-001167 DM-001169 Email string between K. Heffernan and C. Hale	6/16/2014)14 LIFESPAN-0000676		·
Agenda for Meeting of Investigation Committee and Charge to Committee 7/8/2014 LIFESPAN-0001198 LIFESPAN-0001200 Email from Y. Oh to P. Snyder 7/31/2014 LIFESPAN-0000482 LIFESPAN-0000494 Email from C. Saab to C. Saab 8/7/2014 DM-001167 DM-001169 Email string between K. Heffernan and C. Hale	5/19/2014)14 LIFESPAN-0000552	LIFESPAN-0000555	Letter from K. Heffernan to H. Cooper re: allegations
6/25/2014 LIFESPAN-0013839 Committee 7/8/2014 LIFESPAN-0001198 LIFESPAN-0001200 Email from Y. Oh to P. Snyder 7/31/2014 LIFESPAN-0000482 LIFESPAN-0000494 Email from C. Saab to C. Saab 8/7/2014 DM-001167 DM-001169 Email string between K. Heffernan and C. Hale	5/24/2014)14 LIFESPAN-0015578	LIFESPAN-0015579	Email from R. Amabalavanar to P. Snyder
7/31/2014 LIFESPAN-0000482 LIFESPAN-0000494 Email from C. Saab to C. Saab 8/7/2014 DM-001167 DM-001169 Email string between K. Heffernan and C. Hale	6/25/2014)14 LIFESPAN-0013839		
8/7/2014 DM-001167 DM-001169 Email string between K. Heffernan and C. Hale	7/8/2014	L4 LIFESPAN-0001198	LIFESPAN-0001200	Email from Y. Oh to P. Snyder
· ·	7/31/2014)14 LIFESPAN-0000482	LIFESPAN-0000494	Email from C. Saab to C. Saab
Letter from K. Heffernan to C. Hale enclosing recording of Medici's	8/7/2014	L4 DM-001167	DM-001169	Email string between K. Heffernan and C. Hale
8/11/2014 DM-001170 interview before the Inquiry Committee	8/11/2014)14 DM-001170		Letter from K. Heffernan to C. Hale enclosing recording of Medici's interview before the Inquiry Committee
8/11/2014 LIFESPAN-0003052 LIFESPAN-0003053 Email from P. Snyder to J. Murphy	8/11/2014)14 LIFESPAN-0003052	LIFESPAN-0003053	Email from P. Snyder to J. Murphy
8/11/2014 LIFESPAN-0000547 LIFESPAN-0000549 Email from J. Murphy to D. Ormond	8/11/2014)14 LIFESPAN-0000547	LIFESPAN-0000549	Email from J. Murphy to D. Ormond
8/12/2014 LIFESPAN-0004254 LIFESPAN-0004256 Email string between K. Heffernan and G. Brodnicki	8/12/2014)14 LIFESPAN-0004254	LIFESPAN-0004256	Email string between K. Heffernan and G. Brodnicki
8/12/2014 LIFESPAN-0004254 LIFESPAN-0004256 Email from G. Brodnicki to K. Heffernan	8/12/2014)14 LIFESPAN-0004254	LIFESPAN-0004256	Email from G. Brodnicki to K. Heffernan
8/13/2014 LIFESPAN-0004274 LIFESPAN-0004279 Email string between K. Heffernan and G. Brodnicki	8/13/2014)14 LIFESPAN-0004274	LIFESPAN-0004279	Email string between K. Heffernan and G. Brodnicki
9/18/2014 LIFESPAN-0002462 LIFESPAN-0002488 Email from AAAS attaching copy of submitted Walsh manuscript	9/18/2014)14 LIFESPAN-0002462	LIFESPAN-0002488	
9/18/2014 LIFESPAN-0001301 LIFESPAN-0001302 Letter from K. Heffernan to G. Brodnick referring subset of allegation to HMS	9/18/2014)14 LIFESPAN-0001301	LIFESPAN-0001302	Letter from K. Heffernan to G. Brodnick referring subset of allegations to HMS
9/22/2014 Not provided Letter from G. Brodnicki to D. Medici regarding investigation by HN	9/22/2014)14 Not provided		Letter from G. Brodnicki to D. Medici regarding investigation by HMS
9/29/2014 LIFESPAN-0002730 Email from K. Heffernan to C. Hale re: Request for Source Images/D	9/29/2014)14 LIFESPAN-0002730		Email from K. Heffernan to C. Hale re: Request for Source Images/Data
10/3/2014 DM-001201 DM-001204 Letter from C. Hale to K. Heffernan 10/6/2014 DM-001205 DM-001206 Letter from K. Heffernan to C. Hale 11/6/2014 LIFESPAN-0002678 LIFESPAN-0002682 Email form K. Heffernan to G. Brodnicki 11/12/2014 LIFESPAN-0001801 Letter from K. Heffernan to C. Hale 11/12/2014 DM-001214 DM-001216 Letter from K. Heffernan to C. Hale 11/24/2014 DM-001220 DM-001223 Letter from C. Hale to K. Heffernan	10/6/2014 11/6/2014 11/12/2014 11/12/2014	DM-001205 D14 LIFESPAN-0002678 D14 LIFESPAN-0001799 DM-001214	DM-001206 LIFESPAN-0002682 LIFESPAN-0001801 DM-001216	Letter from K. Heffernan to C. Hale Email form K. Heffernan to G. Brodnicki Letter from K. Heffernan to C. Hale Letter from K. Heffernan to C. Hale

Materials Considered by Sheila Garrity, JD, MPH, MBA

<u>Date</u>	Bates Start	Bates End	<u>Description</u>
12/2/2014 12/4/2014 12/5/2014	DM-001224 LIFESPAN-0006823 LIFESPAN-0002862	DM-001225 LIFESPAN-0006825 LIFESPAN-0002864	Letter from P. Shaw to C. Hale Emaul from P. Shaw to C. Hale responding to 12/4/14 letter Email from M. Borreliz to H. Cooper responding to 12/5/14 email
12/9/2014	LIFESPAN-0002310	LIFESPAN-0002314	Email from K. Heffernan to C. Hale re: additional Medici interview
1/9/2015 1/21/2015 2/11/2015 5/20/2015 5/20/2015 5/20/2015 6/4/2015 7/3/2015 8/18/2015 8/27/2015 8/30/2015 9/1/2015	DM-001250 LIFESPAN-0001053 Not provided LIFESPAN-0002193 LIFESPAN-0002191 LIFESPAN-000593 LIFESPAN-0004472 LIFESPAN-0013069 LIFESPAN-0013374 LIFESPAN-0013069 LIFESPAN-0013069	DM-001252 LIFESPAN-0001055 LIFESPAN-0002224 LIFESPAN-0002192 LIFESPAN-0000594 LIFESPAN-0004478 LIFESPAN-0013373 LIFESPAN-0014201 LIFESPAN-0013373	Letter from K. Heffernan to C. Hale Email from P. Snyder to Y. Oh Letter from C. Hale to G. Brodnicki Preliminary Report of the Lifespan Investigation Committee Letter from K. Heffernan to C. Hale Letter from T. Eckford to D. Ramirez Email from K. Heffernan to H. Cooper and C. Hale Medici Respone to Lifespan Investigation Committee's Preliminary Report Final Report of the Lifespan Investigation Committee Medici Response to the Lifespan Investigation Committee's Final Report Letter from J. Kurtis to J. Murphy Letter from K. Heffernan to J. Murphy Email from J. Murphy to P. Snyder re: review of Investigation
9/3/2015	LIFESPAN-0000517		Committee's Preliminary Report and Dr. Medici's Response
9/4/2015	LIFESPAN-0006709	LIFESPAN-0006712	Letter from J. Murphy to Office of Research Integrity re: Notice of Findings and Actions by Lifespan Corporation/Rhode Island Hospital
9/11/2015	LIFESPAN-0000556	LIFESPAN-0000557	Email string between ORI and M. Borreliz re: transmittal of investigation report and related documents
10/26/2015	LIFESPAN-0002583	LIFESPAN-0002585	Email from Peter Snyder to Ranjinidevi Ambalavanar
10/26/2016	Not provided		Harvard Medical School Memorandum re: Report of Inquiry Panel Concerning Allegations against Damian Medici, Ph.D.
6/12/2017 3/1/2018			Second Amended Complaint and Jury Demand Excerpts from Deposition of John Murphy, M.D.

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Materials Considered by Sheila Garrity, JD, MPH, MBA

<u>Date</u>	Bates Start	Bates End	<u>Description</u>
4/6/2018			Excerpts from Deposition of Carl Saab, Ph.D.
5/14/2018			Expert Report of Alan Price
N/A			Medici Dep. Exh. 39 - Thumbdrive images
			42 C.F.R. Part 93

Exhibit 11

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PAGES 1-271

EXHIBITS See Index

1

UNITED STATES DISTRICT COURT FOR THE DISTRICT OF RHODE ISLAND C.A. NO. 17-cv-00265-M-PAS

DR. DAMIAN MEDICI,)

Plaintiff,)

vs)

LIFESPAN CORPORATION,)
RHODE ISLAND HOSPITAL, and)
MICHAEL SUSIENKA,)

Defendants.)

DEPOSITION of MICHAEL J. SUSIENKA, a witness called on behalf of the plaintiff, taken pursuant to the applicable provisions of the Federal Rules of Civil Procedure, before Marie C. Leonard, Registered Professional Reporter, Certified Shorthand Reporter No. 146799, and a Notary Public in and for the Commonwealth of Massachusetts, at the offices of Verrill Dana, LLP, One Boston Place, Boston, Massachusetts, on Tuesday, February 13, 2018, commencing at 10:06 a.m.

KACZYNSKI REPORTING 72 CHANDLER STREET BOSTON, MA 02116

617.426.6060

- 1 Q. Okay. And what type of work did you do when
- 2 you started working for his lab?
- 3 A. A lot of it to start was ordering equipment
- 4 and supplies and reagents to use in
- 5 experiments, because, you know, it was a
- 6 brand-new lab; and there was, you know, some
- 7 equipment available, but we needed, you know,
- 8 new equipment for the lab.
- 9 Q. What -- where was his lab physically located?
- 10 A. In the Coro Building at Lifespan.
- 11 Q. And was her -- his physical lab the same space
- where Mikki's lab had been?
- 13 A. Yes.
- 14 O. Okay. And she had to move out?
- 15 A. Yes.
- 16 O. Where did she move to?
- 17 A. I don't know, somewhere else on the floor
- maybe.
- 19 Q. Did you have any conversation with her in
- 20 connection with her moving out and Dr. Medici
- 21 moving in?
- 22 A. No.
- 23 Q. Did she ever say anything negative about
- 24 Dr. Medici?

- 1 Q. And was she a professor at Brown University?
- 2 A. I believe so or -- yeah, I believe so. I
- 3 don't know.
- 4 Q. Okay. So at -- in August 2013 you had -- you
- 5 had your -- an evaluation, correct?
- 6 MS. WERTHEIMER: Objection. You can
- 7 answer.
- 8 A. Oh. Yes.
- 9 O. Okay. Tell me the -- tell me some more about
- the evaluation you had to undergo in August
- 11 2013.
- 12 A. It's a qualifying exam to propose your -- what
- would be your thesis that you're working on
- 14 for the next few years.
- 15 Q. And what was your proposal for your thesis?
- 16 A. I forget the title. It's in my -- it's in
- the, you know, documents.
- 18 Q. Just like a general description?
- 19 A. It was using synthetic triterpenoids, these
- 20 drugs, to induce endothelial-to-mesenchymal
- 21 transition and --
- 22 Q. Yeah. Why don't we just stop here and she can
- ask you some spelling of words.
- 24 A. Endothelial-to-mesenchymal transition. EndMT

- 1 you recall how long he had been there?
- 2 A. No.
- 3 Q. Was it more than a year or less than a year?
- 4 A. I don't remember.
- 5 Q. David Gonzalez, what was his position?
- 6 A. I think he was an undergrad researcher.
- 7 Q. Was he an undergrad at Brown?
- 8 A. Yes.
- 9 Q. And when -- do you recall when he started in
- 10 his lab?
- 11 A. I don't remember.
- 12 Q. And as of March 31, 2014, was he still in his
- 13 lab?
- 14 A. As far as I know.
- 15 Q. Okay. So at some point, tell me, in August of
- 16 2013, an issue arose with respect to the
- 17 qualifying examination you were doing; is that
- 18 correct?
- 19 A. Yes.
- 20 O. Okay. Just tell me what issue arose.
- 21 A. I had noticed that some of the images that
- 22 Dr. Medici had given me to put into my
- 23 qualifying or he put into my qualifying exam
- for me were duplicates from his -- I think

- from his Nature Med paper, if I remember
- 2 correctly.
- 3 Q. Okay. Tell me, when did he provide those
- 4 images to you?
- 5 A. It would have been, I'm guessing, sometime in
- 6 August of 2013, but I -- the emails would show
- 7 the date he sent that.
- 8 Q. And your understanding is he sent it to you by
- 9 an email?
- 10 A. Yeah. I believe it's -- it's an email.
- 11 Q. And when he sent it to you, how many images
- 12 did he provide to you?
- 13 A. A handful.
- 14 Q. So approximately five?
- 15 A. Five to -- five to seven maybe. I don't -- I
- 16 don't recall.
- 17 Q. And what did he represent those images -- what
- did he represent those images depicting?
- 19 A. That they were depicting triterpenoid-induced
- 20 EndMT.
- 21 Q. And the word you said that began with a tri,
- is that an agent you would treat cells with
- that would induce the EndMT process?
- 24 A. Yes.

- 1 Q. Okay. So did he indicate when the -- that
- process had occurred?
- 3 A. It -- could you clarify the question?
- 4 Q. Well, did he indicate that, These images are
- from a recent experiment I was doing in the
- 6 lab; did he indicate anything along those
- 7 lines?
- 8 A. I believe he said they were from his previous
- 9 lab at Harvard.
- 10 Q. Okay. So was it your understanding he was
- 11 providing those images to you as an example of
- the process that he said they were depicting?
- 13 A. Yes.
- 14 Q. Okay. So he wasn't representing that this is
- something he had just done recently at
- 16 Lifespan, correct?
- 17 A. Correct.
- 18 Q. Okay. And you were going to use those in your
- 19 qualifying exam just for an example of a
- 20 process that you wanted to do your thesis on?
- 21 A. Yes.
- 22 Q. Okay. So what of those images did you
- 23 conclude were -- what was incorrect about
- 24 them?

1 Α. The images were depicting the same cells in 2 what I had presumed was a cell culture dish, and they were identical cells to what was 3 4 depicted in the Nature Medicine paper. 5 And did the Nature Medicine paper represent Q. 6 that the images depicted some other process? Α. Yes. 8 Ο. And what did the Nature Medicine paper 9 represent that the images depicted? 10 Α. I believe it was depicting a different type of I can't recall if it was the growth 11 12 factor one; or I believe there was another 13 figure with endothelial cells that had been 14 transduced to, you know, delete a gene, and 15 that -- I can't recall which figure the Nature Medicine paper -- what -- what images those 16 17 came from, which figure. 18 Q. How did you go about noticing or determining 19 that the images were the same? 20 Α. I was working -- so I had submitted my 21 qualifying exam or my written portion to my 22 committee sometime in August; and then for 23 your actual qualifying examination, there's a 24 presentation portion where you have to give an

1 oral presentation on the -- you know, your 2 proposal; and you typically make PowerPoint 3 slides for this. So it was basically converting that paper, a Word document into a 4 5 PowerPoint format. And I had, you know, the paper open in 6 one window. I had the qualifying exam opened in another, and then I was working on a 9 PowerPoint presentation. And I just happened 10 to notice -- it's pretty glaring -- that the, you know, cells are the same in the two -- two 11 12 images; and it just happened -- I happened to 13 come across it. 14 So you had the -- when you say "the paper," Q. 15 that was the Nature paper? 16 Α. Yes. 17 Okay. And was your proposed thesis -- had --Q. 18 did that have something to do with the EndMT 19 process that was discussed in the Nature 20 paper? 21 Α. No. 22 Okay. Why did you have the Nature paper open? Q. 23 There were other -- it was open just for Α. 24 referencing the methods. There was methods

- were uploaded at Beth Israel?
- 2 A. Yup.
- 3 MS. WERTHEIMER: Objection.
- 4 Q. So is there anything wrong with that statement?
- 5 A. No.
- 6 Q. All right. But you regarded the tone -- you
- 7 regard his response as inappropriate; is that
- 8 a fair statement?
- 9 A. I wouldn't say it was completely
- inappropriate, but it just wasn't completely
- 11 appropriate.
- 12 Q. What did you -- what would an appropriate
- response be, in your opinion?
- 14 A. I don't know.
- 15 Q. You don't know?
- 16 A. It would be more not just replacing incorrect
- images, but also, you know, digging deeper and
- trying to find out what -- what happened and
- then, you know, probably reproducing the data
- to ensure that the images -- the correct
- 21 images are even right.
- 22 O. And after this email exchange, he did return
- 23 from Europe?
- 24 A. Yes.

- 1 Q. And when did he return, approximately?
- 2 A. I don't remember.
- 3 Q. Was it a week or so?
- 4 A. Probably, I don't remember.
- 5 Q. It was prior to --
- 6 A. It was between my qualifying exam and this
- 7 email, so whenever. I don't recall the date
- 8 of my qualifying exam.
- 9 Q. Okay. So it was before the qualifying exam
- 10 date, correct?
- 11 A. Right.
- 12 Q. And then he replaced the images with what he
- regard -- with what he represented as being
- the correct images, correct?
- 15 A. Yeah.
- 16 Q. And as far as you know, those were the correct
- images, correct?
- 18 A. No. There was still a question in my mind as
- to if the images were correct.
- 20 Q. But that's just -- but there's nothing about
- 21 those images -- did you look at those images
- and try and compare them to other papers?
- 23 A. Probably. To make sure -- or just to see if
- 24 they weren't just other like Nature Med paper

- 1 -- the other images in that paper, but --
- 2 Q. Okay. And in that research that you did, you
- didn't find any -- there's no reason that you
- 4 uncovered that those were the incorrect
- 5 images, correct?
- 6 A. Correct.
- 7 Q. All right. So as far as you know, those were
- 8 the correct images, correct?
- 9 A. Yeah.
- 10 Q. Okay. And you took those -- the new images
- and amended your paper and submitted it to the
- 12 qualifying examination committee, correct?
- 13 A. I amended the proposal and the presentation
- itself; but I did not resend the new proposal
- to my committee, at Damian's suggestion.
- 16 Q. The new -- so you amended the proposal but
- 17 didn't submit the proposal?
- 18 A. I had already submitted it with the incorrect
- images.
- 20 Q. Okay. So you didn't submit a new one?
- 21 A. No.
- 22 Q. Okay. And -- but you were ready to submit it
- 23 at the examination?
- 24 A. Yeah. I brought new copies of the proposal.

- 1 Q. And did you verbally represent that what you
- 2 had submitted, there is some incorrect images?
- 3 A. No.
- 4 Q. And why not?
- 5 A. Because Dr. Medici told me not to, only to
- 6 bring it up if somebody asked.
- 7 Q. Okay. And was that -- did you pass that
- 8 examination?
- 9 A. Yes.
- 10 Q. And did they regard that as an appropriate
- 11 subject for a thesis?
- 12 A. I assume so.
- 13 Q. Okay. Now, do you feel like you misled -- was
- it a committee that was -- you were speaking
- in front of, or who were you speaking in front
- 16 of?
- 17 A. Committee, yeah.
- 18 Q. Okay. Did you feel like you misled the
- 19 committee?
- 20 A. No.
- 21 Q. Do you feel like Dr. Medici was inappropriate
- in the advice he gave you?
- 23 A. In retrospect, yes.
- 24 Q. At the time did you feel that it was?

- duplications and in some cases triplications
- among his manuscripts and published papers.
- 3 Q. When did you -- how did you go about doing --
- 4 when did you start looking at his other
- 5 manuscripts and published papers?
- 6 A. I don't recall exactly. Probably in the
- 7 February, March time frame again.
- 8 Q. Okay. So in August when an issue arose, that
- 9 didn't prompt you to then look at his other
- 10 papers; is that a fair statement?
- 11 A. Correct.
- 12 Q. Okay. But sometime did you say in February
- you started looking at his other papers; is
- 14 that a fair statement?
- 15 A. Correct. Yes.
- 16 Q. Was there anything that prompted you to do it
- 17 at that time?
- 18 A. There was the STAP stem cell controversy,
- 19 S-T-A-P, that was in the news at that time,
- and there was a sim -- there was a lot of
- 21 image duplications and issues with those
- papers that were, you know, uncovered.
- 23 O. And was that in Japan?
- 24 A. I believe so.

- 1 Q. Okay. And that was in the general news or
- just the scientific news?
- 3 A. I think both.
- 4 Q. Okay. And just tell me briefly what that
- 5 controversy was.
- 6 A. Basically this lab at Harvard and Japan were
- 7 collaborating on this method to easily induce
- 8 pluripotency into non-stem cells and turn them
- 9 into stem cells. And it seemed too good to be
- 10 true; and there was a lot of, you know,
- investigations into it, and they found image
- 12 duplications in -- I forget if it was in that
- exact manuscript or that exact paper or other
- papers published by that -- you know, those
- authors.
- 16 Q. Okay. So, and then did someone, like, kill
- 17 themselves over it; is that what happened?
- 18 A. I believe somebody committed suicide.
- 19 Q. Was that in the news at that time point?
- 20 A. I don't recall.
- 21 Q. All right. So prior to that, had you had
- 22 heard about research misconduct involving
- images that were duplicate images?
- 24 A. Yes.

Exhibit 12

From: Medici, Damian <damian_medici@brown.edu>

To: Michael Susienka **Sent:** 9/28/2013 10:13:35 PM

Subject: Sheridan Letter

Hey Mike,

The letter is attached. Have a look and let me know whether it is sufficient or if you think something should be added. If it looks good to you, go ahead and submit it and the proposal.

Best,

Damian



Rhode Island Hospital

I Low of the Post in t

Principles and Practice in Reflective Mentorship Initiative The Harriet W. Sheridan Center for Teaching and Learning September 26, 2013

To whom it may concern,

I am pleased to provide my strongest and most enthusiastic support to Michael Susienka and David Gonzalez for the Harriet W. Sheridan Center for Teaching and Learning Mentorship Award. I am also delighted to serve at their senior advisor for their proposed project entitled "Role of the Skeletal Muscle Microenvironment in Heterotopic Ossification." As Assistant Professor of Orthopaedics and Medicine at the Warren Alpert Medical School of Brown University and Director of the Laboratory for Regenerative Medicine at Rhode Island Hospital, and an established expert in the field of study that Michael and David are pursuing, I feel that I am highly qualified to provide them with the necessary guidance to ensure that their project is a success. I will also cover any costs for laboratory supplies not outlined in their budget.

I believe that Michael and David are highly qualified to conduct the experiments outlined in their project proposal. As a third-year Ph.D. candidate in the Graduate Program in Biomedical Engineering with experience in mechanical testing, Michael has the engineering expertise required for the mechanical stimulation and more quantitative aspects of the proposal. David, as a senior undergraduate student in Biochemistry and Molecular Biology, has in-depth knowledge of the more biological aspects of the proposal, such as gene expression and cell signaling. I believe that Michael will be an excellent mentor for David; in fact, he has already taken on that role of his own accord since David started in my laboratory last semester. Their unique backgrounds in scientific research will compliment each other well to maximize the potential success of their project.

Although his graduate program only requires Michael to serve as a teaching assistant for one semester, I have encouraged him to teach as many classes as possible so that he can develop important mentoring skills that will be critical to his career, particularly if he decides to stay in academia. Additionally, I have urged him to enroll in the Sheridan Teaching Certificate I program next year to further develop his teaching skills.

I see bright futures for both Michael and David. They are both highly motivated students who are truly passionate about scientific research. With his strong academic records and experience in biomedical research, I am certain that they will be outstanding representatives of the Sheridan Center. If you have any questions, please feel free to contact me at any time.

Sincerely.

Damian Medici, Ph.D.

Assistant Professor of Orthopaedics and Medicine Warren Alpert Medical School of Brown University Director, Laboratory for Regenerative Medicine

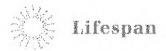
Rhode Island Hospital

1 Hoppin Street, Coro West, Suite 402C

Providence, RI 02903 Tel: 401-444-7180 Fax: 401-444-5006

Email: damian_medici@brown.edu

Exhibit 13



CONFIDENTIAL

Interview by Lifespan's Inquiry Committee (Drs. C. Saab (Chair), V. Knopik, M. Carey, & A. Ayala) **RE**: Allegations of Research Misconduct in Dr. Damian Medici's laboratory

Damian Medici April 21, 2014 10:30am-11:40am Coro West, 1,309	
Comparison of two papers (slide-set) there is a slight from each lesson that seems a little too close to call different. In our position, what would you have said about this?	Comment [v1]: ? Should this be "slide from each paper or manuscript"? Or a "site from each Western (blot)"?
cross	Comment [v2]: ?
onePlos One	Comment [v3]: ? should this be "separate"
Do you remember if these were used in a thesis?	
Do you remember the source? There were many authors on the paper.	
So you agree with us that this looks the same?	
Ok, so I'm hearing three conclusions: 1) you think they're similar 2) you don't know the source of these lessons, whether you did them or someone else, and 3) they were both generated at Harvard	Comment [v4]: Westam?
If you can think of anything else in the meantime.	Comment [v5]: Until?
So when you say, you published, meaning as a group, or it went from your lab after you came here?	
Comparison of two papers (slide-set) – showing lessons	Comment [v6]: Western?
The one on the top is from the plus <u>PLos one One</u> paper and the one on the bottom is from the 2012??.	
So, assuming these are similar, do you know the source of these data?	

Were you first or last author on either of these papers?

Page 2 of 7
IDENTIAL.

	When you say came out? It was a collaboration?
ı	(external
ı	collaborator at?)
ı	2011 figure 1 (Journal) and we have figure 2 from 2012 (Journal).
	The interesting thing is they were both in the same article.
	When a paper is published, different lab, different transcribe. It's important for us for that you to tell us Comment [v7]: 9
	what your contribution was.
	(Instructor @ Harvard)

You were a graduate student at some point, you must've produced data.

Comparison (slide-set): 2011 supplemental figure 3 (<u>Journal</u>) and from <u>matrix PenelopeMatrix Biology</u> 2011 supplemental and we will ask you about these (slides) as well.

The concern to us is that they're not duplicates of the same condition; they're duplicates of presumably different conditions. This is a major difference; this is a publication in revision or we think it's in resubmission we're not sure. These are some of the data we gathered from the people from the lab, sometimes we were given unpublished data that are in the process of being submitted or being revised, so we can't really tell what stage this is at, but we were concerned to see the following (slide-set). We think these are also the same.

Can you tell us whether this is the latest version of what you have (slide: right side panel) or has this been edited and resubmitted somewhere else as something else. We don't have the latest. But even if this was submitted and rejected, this is very troubling. Not a good thing.

We need to keep track of all of these as they go in for resubmission.

is

We don't know what stage this at. We asked people in the lab about electronic copies, not a lot of people have copies of their own publications, we were told that they were handed hard copies to write notes on and return them back to you. Slide: this is another one in publication/revision (which one?).

This isese mostly publication related issues that we have, it waswere enough for us, that it prompted us to have a conversation with you about research in your lab, style of research, who is in your lab, who is working, who is doing what, how do you allocate experiments. To talk about your projects.

Hartford Harvard

Page 3 of 7
CONFIDENTIAL

	Can you walk us through a little bit about what was your main, flagship project when you came here and what has your lab achieved so far? Can you tell us a little bit of the data that you're producing here?		
	Is this related to your inertia Nature paper? Could you rank these, in terms of importance to you? ossification oscification How is this done (we're not experts)?		
1	matchspec-Mass Spec(trometry)	Comment [v8]: Cell types?)
1	The strategy would be?		
	Are you involved in these experiments at all, hands on work?		
	Do you keep a lab notebook for yoursell?		
١	<u>गांद</u>		
	Can you describe your relationship with all the lab members, and elaborate on each one of them?		
	Let's start with the assistants first.		
	Her task, her job, what is she good at, has she been able to accomplish the projects that you hand over to her, when did she come to the lab?		
	She was one of your first hires?		
1	What is Mike's backgraound?		
	What lab was that?		
	So, she is a Ph.D.?		
	Do you know what Mike's role was in that lab?		
	What did you like about him?		

COL	Page 4 of 7 NFIDENTIAL
Skilled in what way?	
How would you rank him so far?	
Has there been any issues with Michael since he came to your lab? I'm going to ask the san about every single one of the lab members.	ne question
(Olin)	
Where do you run your mathvac (?), here?	Comment [v9]: Mass Spec? Formatted: Highlight
How long has she worked on this project for?	(Formacted: nig night
So, for the past two years or so there hasn't been any production or failing finding good encepaper?	ough for a Formatted: Highlight
But otherwise, you would think that the performance of everyone in the lab is up to your sta	undard?
Who guided the initial training? (Liang)	
When did he come?	
Again refresh my memory, the	
And you said he's trying to or is that something new?	
Where he is at that stage, has he been able to make transformation?	
Fit proves produces as a	
So, did you	

1

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telepoint PowerPoint (at Harvard) How were you at Harvard? Comment [v10]: Funded? So the RO1 was initiated there and then transferred here? When we talked to Diana and Melissa, I can't remember which one of them, they claim that they were also involved in this project Were they playing a supportive role or were they doing independent things? DM: Independent things. I was working on trying to convert endothelium into skeletal myocites myocytes Formatted: Font color: Custom Color(RGB(79,129,189)) and Melissa was trying to work on converting into neurons. We got some morphological confirmation that seemed to work but the biochemical confirmation didn't seem to be Formatted: Font color: Custom Color(RGB(79,129,189)) working, still trying to work out the bugs on that. So personally, when I listen to them, I'm concerned that they spend most of their time in the lab trying to do this and have been unsuccessful so far or is this something that you are an expert in and able to do this and publish on it. Did you step in at any point and try to help them with this? DM: Yes. When people struggle with stuff I try to go in and help. Formatted: Font color: Custom Did it work? Formatted: Font color: Custom DM: It seemed to work for me, it worked for Melissa. Color(RGB(79,129,189)) Do you have timestamps for these experiments? DM: Should be in her notebook. She treated cells with -Formatted: Font color: Custom bleomycin before. Color(RGB(79,129,189)) How long ago? DM: Probably like a year ago. Melissa technically moved into Tony lab, she's not really Formatted: Font color: Custom Color(RGB(79,129,189)) mine (under DM's direction), she was just like an intern on paper, a research assistant for me. She was a volunteer? DM: Exactly Formatted: Font color: Custom Color(RGB(79.129.1893) who is a friend of mine, needed a research assistant, so we set that up so she Tony could work for him, she's been primarily working for him since then ... I think that was August of last vear She was in your lab between what period? DM: I believe it was either November or December of 2012; it was shortly after Diana joined the lab, Formatted: Font color: Custom Color(RGB(79,129,189)) they're sisters, you knew that. I guess they're both in medical school and wanted research experience in order to do that. I told her I didn't have the money, I only had the money to cover one research assistant, so I could only hire Diana. So I said one could intern. When did she go to Tony lab? DM: I believe it was August of last year. But Tony and I have been collaborating on this project on Formatted: Font color: Custom Color(RGB(79,129,189)) transition and basically skin fibrosis, since we collaborate, schleraderma and Melissa does a lot of the stuff that she does for Tony in my lab and I was fine with that. You can use my reagents, do whatever you want to. We're trying to understand where the data is coming from, that's why we're asking you all of these questions. Some of the data comes from the assistants, students, some from you. You put the matchstick manuscript together. You said nothing that you've generated since you came here has been published, it's

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not even in consideration for publication anywhere, could be in grants or anything. It's very important that you follow up. If you generated anything here that you think is suspicious that you share it with us. DM: I don't think anything here is suspicious. The fact that this stuff was done so long ago, privy prior (to coming) to this institution, I'm not there (Harvard) anymore, the people that were working for me are not there anymore.

Formatted: Font color: Custom Color(RGB(79,129,189))

2012 is not that old	
DM: Well, that's when it was published. The vast majority of that stuff was done when I was a graduate	Formatted: Font color: Custom Color(RGB(79,129,189))
student or post-doc. A lot of that stuff we basically sat on. Even the paper that you showed (WelshWalsh), was mostly done, he was there summer of 2009, this was five years ago, we basically sat on this stuff because we figured there was no way it was going to get published if there wasn't any	Formatted: Font color: Custom Color(RGB(79,129,185))
experimentation. Problem with this stuff on and all of this is that there is no animal model. You've been working on this though, recently, injecting tumor cells in mice?	
DM: Not tumor cells, that doesn't work. We've been actually trying to create a mouse model of that by taking resected tissue from patients cutting it into pieces and inplanting into immune deficient mice and they do sort of grow for a little bit and then they do sort of naturally regress	Formatted: Font color: Custom Color(RGB(79,129,189))
which follows the natural progression of the tumors, but the problem with the that is that now we're using a drug called which basically eradicates these tumors in the patients. When I was at	
Harvard we would get maybe one patient specimen every month, now we're lucky if we even get one	
patient specimen every year and if we do get a patient specimen its usually so small that we can't do	
enough experiment that get statistically significant data. Like with these old paper on If	
there's not enough data, it's probably not going to be published anyway.	
At some point, was there someone working in the lab who was resident from European country, your lab?	
DM: Who? Oh Luciana (Jorna). She was from the Netherlands, she was a master's student over in the	Formatted: Funt color: Custom
Netherlands, she worked for some people I collaborate with over there, Martinand	Color(RGB(79,129,189))
there's a cardiovascular lab over there, basically as a favor to my friends, apparently	
students, externship, she came over here for about six months, she did some work looking at basically	
what they look at over in the Netherlands in that group. She was sort of looking at angiogenesis	
Nothing that was really innovative. Most of it was already sort of known.	
In spite of it, she was named as first author	(=
DM: Authorship, I receive for intellectual contribution. We sort of designed the project together in collaboration with the group in the Netherlands.	Formatted: Font color: Custom Color(RGB(79,129,189))
Was she able to finish her project before she left?	Formatted: Font colo : Custom
DM: For the most part, yea.	Color(RCB(/9,129,18S))
4/30/14: FOLDER B: 21:52 (NOT COMPLETE)	Formatted: Font color: Custom Color(RGB(79,129,189))

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Exhibit 14

From: Medici, Damian <damian_medici@brown.edu>

 To:
 Michael Susienka

 Sent:
 8/7/2013 5:26:11 PM

Subject: Qual

Brown University
Department of Molecular Pharmacology, Physiology and Biotechnology
Center for Biomedical Engineering
Graduate Program in Biomedical Engineering

Qualifying Examination

Endothelial-mesenchy	ymal transition t	for cartilage regenera	tion

Michael Susienka

August 22, 2013

Thesis Advisor: Damian Medici, Ph.D.

Qualifying Examination Committee:Ruhul Abid, MD, Ph.D.Eric Darling, Ph.D.lan Wong, Ph.D.

Statement of Hypothesis and Specific Aims

Fibrodysplasia ossificans progressiva (FOP) is a debilitating disease in which inflammation in soft connective tissues (muscle, tendon, etc.) causes them to die and be replaced by cartilage, which is then remodeled into bone. This heterotopic ossification (HO) occurs through a process known as endothelial-mesenchymal transition (EndMT), wherein vascular endothelial cells are transformed into mesenchymal stem-like cells, which give rise to the heterotopic skeletal cells. FOP is caused by an activating heterozygous germ-line mutation (R206H) in the activin-like kinase 2 (*ALK2*) gene, which encodes a transforming growth factor beta (TGFβ)/bone morphogenic protein (BMP) type 1 receptor. Activation of this receptor with ligands such as BMP2 or BMP4 induces EndMT and heterotopic ossification in mice. Drugs known as synthetic triterpenoids have been shown to promote the expression of BMP2 and induce chondrogenesis. **Our long-term goals are** to identify the mechanisms of synthetic triterpenoids in inducing EndMT-dependent chondrogenesis and to use these drugs to regenerate articular cartilage for the treatment of osteoarthritis (OA).

Our preliminary data suggest that triterpenoids induce EndMT and subsequent chondrogenesis in a BMP-2-dependent manner. Interestingly, conditionally knocking out BMP2 in the limb buds of mice inhibits the natural process of skeletal tissue regeneration during bone fracture healing. Therefore, we hypothesize that BMP2-dependent EndMT generates chondrocytes as a natural mechanism of skeletal tissue regeneration and can be recapitulated to treat OA.

We intend to test this hypothesis with the following specific aims:

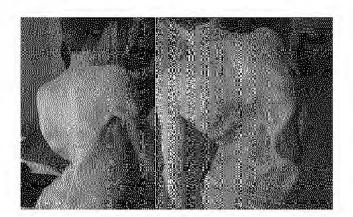
Specific Aim 1: To determine whether BMP2-dependent EndMT will generate chondrocytes during fracture healing. We intend to test...

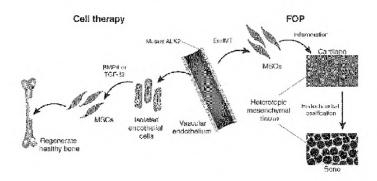
Specific Aim 2: To regenerate articular cartilage for the treatment of OA using synthetic triterpenoids to induce EndMT and chondrogenesis. We will assess...

Specific Aim 3: To identify the signaling mechanisms that cause triterpenoid-induced expression of BMP2. We will...

Research Strategy

Significance





*Add Medici and Sporn paper figure on calvaria

Innovation

This project is innovative....

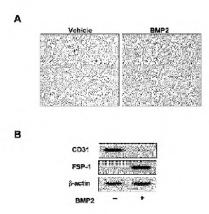
*Add schematic diagram

Research Design and Methods

Specific Aim 1: To determine whether BMP2-dependent EndMT will generate chondrocytes during fracture healing.

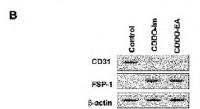
Our preliminary studies demonstrate that...

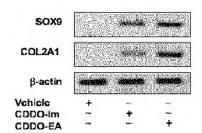
*Add Tie2 staining of fracture callous

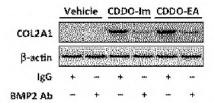


Specific Aim 2: To regenerate articular cartilage for the treatment of OA using synthetic triterpenoids to induce EndMT and chondrogenesis.

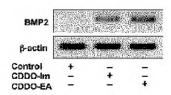
Control CDDO-Im CDDO-EA







Specific Aim 3: To identify the signaling mechanisms that cause triterpenoid-induced expression of BMP2.



*Add blots for Phospho-ERK1/2

*Add kinase array images if you have them

Expected outcomes

Aim1. It is expected that

Aim2. We expect that

Aim3. We expect that

Alternative Approaches

If any problems occur...

Statistical Analyses

Statistical analyses for all experiments proposed in Specific Aims 1, 2, and 3 will be performed using one-way analysis of variance (ANOVA) and/or two-tailed paired student's t test using GraphPad Prism 6.0 software. Probability values less than 0.05 will be considered significant.

Proposed Timeline

References

Exhibit 15

From: Medici, Damian <damian_medici@brown.edu>

To: Susienka, Michael **Sent:** 8/17/2013 7:12:59 PM

Subject: Qual

1) Calm down

- 2) I will look at this as soon as I return. If you are correct then i'm going to be extremely pissed off at my former postdoc for sending those images. Mistakes happen all the time in this field and they can be easily corrected. Whether this was done maliciously, i dont know but i will find out. We were all in a panic to finish your qual by the deadline its more likely that this was just a screw up. All of our data files were uploaded onto our lab server at Beth Israel so all of my lab members had access to them and most of them weren't labeled very clearly usually with abbreviations and number codes. Hopefully this is just a mistake and some of the files got mixed up or they were looking at my old files thinking they were different ones.
- 3) We are not going to publish those data.
- 4) Those data are not yours so you are not directly responsible for them.
- 5) Don't tell anyone about this. This sort of thing can get blown out of proportion very quickly and do severe damage to both your career and my career. Trust me, I take this more seriously than anyone, and the most important thing is that everything that comes out of our lab is legit. The first thing we should do is meet as soon as i return to go over this and decide the best course of action. I will call you as soon as i get back to the states. Just keep preparing your presentation. If those images are incorrect we will replace them with the correct ones. I promise we will fix this and everything will be ok.

D

On Saturday, August 17, 2013, Susienka, Michael wrote:

When I was working on my presentation the other night, I noticed something very troubling about some of the figures that you provided for my research proposal. More specifically:

- In my Figure 6A, the Vehicle image is the same as the HUVEC Vector image in Figure 2C of your Nature Med paper.
- In my Figure 7A, the Control image is the same as the HCMEC WT image in Figure 2C of your Nature Med paper.
- In my Figure 7A, the CDDO-Im image is the same as the HUVEC Mut image in Figure 2C of your Nature Med paper.

I wasn't able to find any other duplicate images; however, to be honest, all of the other unpublished figures you gave me are now suspect, unfortunately.

I'm not sure who is responsible for this, but I'm completely shocked/dumbfounded right now. I absolutely do not feel comfortable presenting these figures as preliminary data and feel deceived/embarrassed that I put my name on a research proposal with this blatant misrepresentation of data.

I have no idea how to proceed.

Mike

On Fri, Aug 16, 2013 at 7:41 PM, Medici, Damian <damian_medici@brown.edu> wrote: I didn't bring my laptop so it'll be difficult to Skype or gehat. Can you just email me the questions and I can get back to you when I'm hooked up to wifi?

Thanks,

D

On Friday, August 16, 2013, Susienka, Michael wrote: Hi Damian,

I have a few questions about a couple of the figures in my QE research proposal.

If possible, I'd like to discuss this over phone/Skype or Gmail voice chat. Let me know when you are available.

Thanks, Mike

Michael Susienka Graduate Student, Biomedical Engineering Brown University --

Michael Susienka Graduate Student, Biomedical Engineering Brown University

Exhibit 16

From: Brown Grad Student

Browngradstudent1@yahoo.com>

 To:
 psnyder@lifespan.org

 Sent:
 3/31/2014 5:59:12 PM

Subject: Files

Hi Dr. Snyder,

Thank you again for meeting with me today. I really appreciate it.

Please find attached the files you requested. Let me know if there's anything else you need.

Michael

Supplementary Information

Endothelial-mesenchymal transition promotes the natural regression of infantile hemangiomas

Logan A. Walsh¹⁻³, Diana Ramirez⁴⁻⁷, Melissa Ramirez⁴⁻⁷, John B. Mulliken⁸ & Damian Medici^{1,2,4-7}

¹Division of Matrix Biology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02115, USA.

²Department of Developmental Biology, Harvard School of Dental Medicine, Harvard Medical School, Boston, MA 02115, USA.

³Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, USA.

⁴Department of Orthopaedics, Warren Alpert Medical School of Brown University, Providence, RI 02903, USΛ.

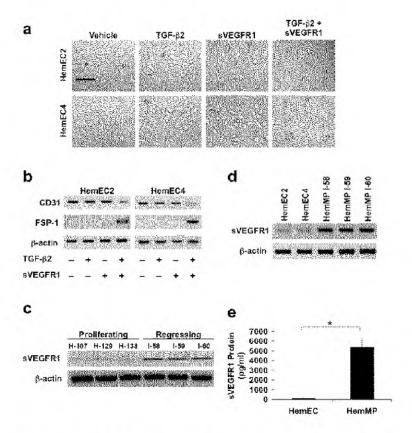
⁵Division of Hematology/Oncology, Department of Medicine, Warren Alpert Medical School of Brown University, Providence, RI 02903, USA.

⁶Laboratory for Regenerative Medicine, Rhode Island Hospital, Providence, RI 02903, USA.

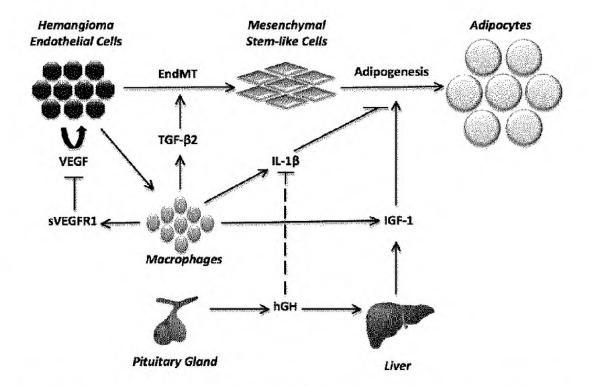
⁷Cardiovascular Research Center, Rhode Island Hospital, Providence, RI 02903, USA.

⁸Department of Plastic and Oral Surgery, Boston Children's Hospital, Harvard Medical School, Boston, MA 02115, USA.

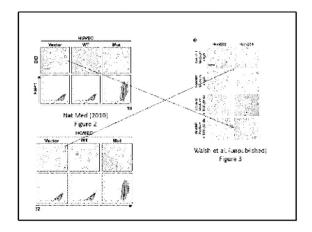
Correspondence should be addressed to Dr. Damian Medici (damian medici@brown.edu)

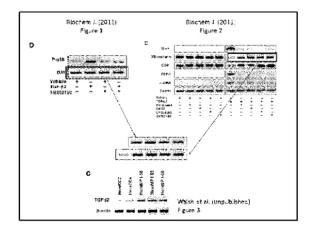


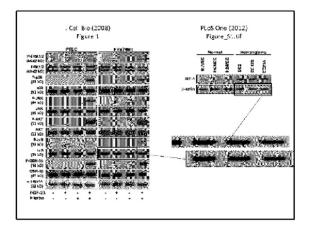
Supplementary Figure 1 TGF-β2 stimulates EndMT of hemangioma endothelial cells when VEGF signaling is inhibited. (a) DIC imaging showing that TGF-β2 alone was insufficient to induce EndMT of hemangioma endothelial cells (HemEC), but a combination of TGF-β2 and sVEGFR1 permits EndMT. Scale bar, 20μm. (b) Immunoblotting showing that TGF-β2 and sVEGFR1 promote decresed expression of the endothelial marker CD31 and increased expression of the mesenchymal marker FSP-1. (c) Immunoblotting showing that regressing hemangiomas (I-58, I-59, I-60) have higher expression of sVEGFR1 than proliferating hemangiomas (H-107, H-129, H138). (d) Immunoblotting showing that HemECs express little sVEGFR1, whereas hemangioma macrophages (HemMP) produce high amounts of sVEGFR1. (e) ELISA analysis of secreted sVEGFR1 from HemECs compared to HemMPs. Data represent mean (n=3) \pm s.d.; *P<0.01 by t test.

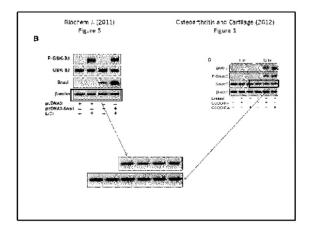


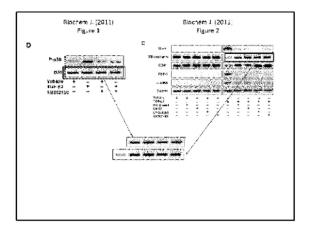
Supplementary Figure 2 A schematic diagram of the proposed mechanism of hemangioma regression. Hemangiomas arise by constitutive VEGF signaling. Macrophages infiltrate the tumor over time and secrete sVEGFR1, which binds and sequesters VEGF to inhibit proliferation. This inactivation of VEGF also allows EndMT induction by TGF-β2 secreted from macrophages. These newly formed mesenchymal stem-like cells are differentiated into adipocytes by IGF-1 that is produced by the infiltrating macrophages, but can also be blocked by IL-1β. Since patients with infantile hemangioma are children with systemically high levels of hGH, IL-1β production from macrophages is inhibited by the hormone. Also, hGH primarily targets the liver to induce production of the adipogenic cytokine IGF-1, suggesting that systemic hGH may have a two-fold effect on mediating hemangioma regression.











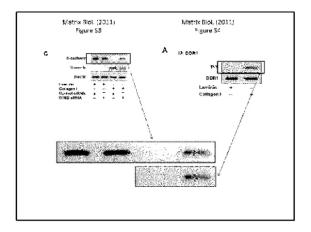


Exhibit 17

From: Rosenberg, Ruth Kohom <ruth_kohorn_rosenberg@brown.edu>

To: brown Grad Student
Sent: 3/7/2014 12:06:31 PM
Subject: Re: Appointment

Hi

Beth Harrington is the associate dean for graduate and postdoctoral studies in biomed, so probably another person to consider talking to.

Here is the policy on reporting on allegations of research misconduct

It also talks about protecting people who make complaints and also provides a way of talking informally to the Research Integrity Officer (Regina White) to see what the next steps might be:

http://brown.edu/research/about-brown-research/policies/policy-responding-allegations-research-misconduct

Regina White is away until 3/17.

Ruthy

"Kindness is in your power, even when fondness is not." Samuel Johnson

Ruthy Kohorn Rosenberg, University Ombudsperson Brown University RuthyK@brown.edu or 401-863-6145 www.brown.edu/ombudsperson

The University Ombuds Office is an independent, neutral, confidential and informal resource for conflict management. The Ombuds Office does not accept formal complaints or notice for Brown University, nor does the office retain records of confidential communications; communications with the Ombuds Office are considered off the record. Please remember that email is not appropriate for confidential communications.

On Wed, Mar 5, 2014 at 3:21 PM, Rosenberg, Ruth Kohorn < ruth_kohorn_rosenberg@brown.edu> wrote:
Hi

I will see you at 10 am this Friday 3/7. I'm on the third floor of the Hillel Building at the corner of Angell and Brown streets

Ruthy

"Kindness is in your power, even when fondness is not." Samuel Johnson

Ruthy Kohorn Rosenberg, University Ombudsperson Brown University RuthyK@brown.edu or 401-863-6145 www.brown.edu/ombudsperson

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On Wed, Mar 5, 2014 at 3:17 PM, brown Grad Student < <u>browngradstudent1@yahoo.com</u>> wrote: Hi Ruthy,

Friday morning at 10am would work best for me.

Thanks!

On Wednesday, March 5, 2014 1:45 PM, "Rosenberg, Ruth Kohorn" < ruth_kohorn_rosenberg@brown.edu > wrote: Hi

tomorrow, Thursday at 3:30 Friday morning before 11:30

next week Tuesday at 10 or 10:30 Thursday between 10:30 and 1, or Friday at 1 or 1:30

let me know if there's anytime in there that works for you

Ruthy

"Kindness is in your power, even when fondness is not." Samuel Johnson

Ruthy Kohorn Rosenberg, University Ombudsperson Brown University RuthyK@brown.edu or 401-863-6145 www.brown.edu/ombudsperson

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On Wed, Mar 5, 2014 at 1:39 PM, brown Grad Student < browngradstudent1@yahoo.com > wrote: Hello.

I would like to make an appointment to meet with you sometime this week or next about a situation involving potential academic misconduct. Anytime works for me.

Thank you.

Exhibit 18

Lifespan

April 1, 2014

Research Integrity Claim, regarding Dr. Damian Medici

. Meeting with Michael Susienka on 31 March 2014

Mr. Michael Susienka, a third year biomedical engineering Ph.D. student at Brown University met with me in my office (Coro West, 1st floor, suite 1.001) yesterday afternoon, accompanied by Dr. Elizabeth Harrington (Associate Dean for Graduate Education, Alpert Medical School). Dr. Harrington, in consultation with the vice president for research at Brown, Dr. David Savitz, determined that this potential claim against one of our professors, Dr. Damian Medici, should be managed through my office as he is an employee within Rhode Island hospital and maintains his laboratory on the fourth floor of Coro West.

Mr. Susienka had previously trained with Dr. Mickey Ciombor for a little over one year, but for the past fifteen months or so he has worked under the supervision of Dr. Medici in the orthopedics laboratories. Mr. Susienka had finished his undergraduate degree at Western Polytechnic Institute, and he is currently a fully matriculated Brown University graduate student.

Mr. Susienka describes Dr. Medici as having a difficult to control temper, a "huge ego", and that he perceives Dr. Medici to be "somewhat paranoid". Apparently, Dr. Medici has bragged in laboratory meetings that he had been arrested for bar fights and Mr. Susienka suspects that he may have used a prior name (Damian Lagamba) and that he believed that there are four prior publications with Dr. Medici's former graduate mentor, with that name. This raises the possibility that Dr. Medici may currently be using an alias for unknown reasons. All of this remains unsubstantiated at present. Mr. Susienka notes that Dr. Medici has his home address and he stated on multiple occasions that he is very concerned for his personal safety. Specifically, he is worried that by coming forth with concerns about potential research conduct improprieties, that Dr. Medici will seek retaliation against this claimant, and Mr. Susienka repeatedly described concerns for his personal safety and worries about physical violence. When probed further, this student expressed concerns that Dr. Medici might be so angry with him that he may stalk and physically accost this student outside of the workplace. For this reason, in managing this case moving forward, I would like to provide a month or more for a silent review of evidence by any investigative committee to be formed, with private interviewing of this claimant, to allow him time to seek supervision in a new laboratory in order to finish his PhD program, and to consult with attorneys about how to proceed while still ensuring personal safety for this claimant to the best of our ability.

I made it very clear to Mr. Susienka that there will undoubtedly be a point in time during this investigation, in which Dr. Medici will be made aware of these claims and concerns, so that he may be properly interviewed by an investigative committee and so any potential laboratory evidence might be sequestered and examined by that committee. Dr. Medici deserves equal right to present his views and to support his own work and case, and by doing so these claims will be made known to him. Mr. Susienka understood that this will happen at some point within the next few months, and he specifically asked that this investigation proceed per institutional research

Peter J. Snyder, PhD Senior Vice President and Chief Research Officer

Research Administration Coro West One Hoppin Street 1st Floor, Suite 1.001 Providence, Ri 02903

Tel 401 444-4117 Email psnyder@lifespan.org

Professor Department of Neurology The Warren Alpert Medical School of Brown University

Adjunct Professor Child Study Center Yale University School of Medicine

Senior Associate Editor, Alzheimer's & Dementia: The Journal of the Alzheimer's Association



integrity policy. I agreed to let Mr. Susienka know when this process would reach a point at which Dr. Medici would become aware of a probable investigation.

Mr. Susienka has been a student in the Medici lab since August 2012 working on the topic of cartilage regeneration and fraction healing. He believes that his position in the laboratory is funded by the University Orthopedics foundation, rather than a direct line on a federal grant. Dr. Medici's work is funded through the Orthopedics COBRE center as well as at least RO1 grant that Dr. Medici has as the principal investigator. Of note, the RO1 grant and work through the COBRE center may be unrelated to Mr. Susienka's specific graduate project.

Mr. Michael Susienka prepared and completed his qualifying exam in the summer of 2013, producing a ten page research proposal under Dr. Medici's guidance. In preparation of his qualifying written examination, Dr. Medici provided Michael with figures that he believes were supplied by a former "post-doc of Dr. Medici's at Harvard". Dr. Medici instructed Michael to use these figures to support his proposal, and in doing so Michael noticed that these figures were listed from a prior publication that described an entirely different study with different treatment. That is, these blots were apparently supposed to provide preliminary results in support of Michael's proposal with Luten experimental paradigm, but these figures were from a publication with old data using a completely different paradigm. Michael described feeling "horrified" when he noticed this error, and he sent an email to Dr. Medici who was traveling oversees at the time to ask how this could've happened. Apparently, Dr. Medici claimed that this must've been a clerical error of sorts and instructed Mr. Susienka in email "never to say anything to anyone about this".

Subsequent to this event, Dr. Medici sent new images which appeared to Mr. Susienka to be legitimate, although Michael is unsure of the providence for those images. Michael then passed his qualifying exam and has been working in the Medici lab up to the present point. His experience while completing the qualifying exam led him to review papers of Dr. Medici's, both older ones as well as two manuscripts which are currently submitted and under review to different journals, and in several of these papers he found additional instances of republishing old work in completely new context. Specifically, Mr. Susienka believes he found four separate instances of data fraud, with one of them occurring within a manuscript currently under review that bears Mr. Susienka's name as a co-author, as well as the Rhode Island hospital institutional affiliation for Dr. Medici. In this manuscript under review, Mr. Susienka claims that Dr. Medici is using old data in a completely new context and he has provided the graphic and written evidence for any investigative committee to review. In addition, Mr. Susienka is concerned that in his experience the experiments on campus that support this manuscript actually failed, and once this was clear Dr. Medici took biologic tissue prepared here and then brought the tissue to Harvard to potentially a former laboratory that he was affiliated with; Dr. Medici then came back to the local lab group with completely processed results embedded already within the manuscript and claimed success of the experiment to his lab group. Again, Dr. Medici apparently ran all of these analyses himself off of the campus and then came back with no raw data available. Mr. Susienka suspects that these data may be either fraudulent or falsified, and he is afraid to ask to have his name removed from the manuscript, again because of fear of retaliation. Mr. Susienka is unsure whether the data in this current paper are real or false.

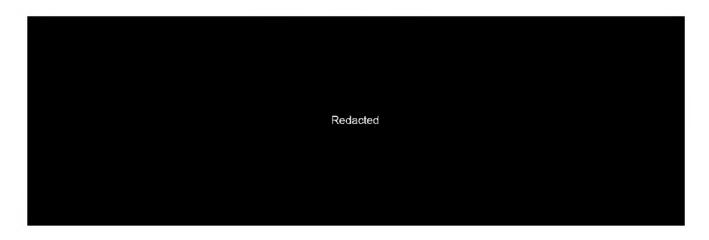
Dr. Medici is currently up for promotion at his time, and Mr. Susienka notes that his application has been temporarily stalled in the dean's office, as Dean Elias may feel that Dr. Medici has not

published enough high quality papers during his tenure within the Brown system. This means that Dr. Medici and his lab group are under intense pressure to publish and Mr. Susienka is concerned that this means the work is becoming sloppy and that there may be research improprieties occurring as described above. Mr. Susienka does think he can pursue a PhD in this laboratory and is looking to make a transfer. Associate Dean Harrington is assisting him in this regard.

Mr. Susienka is supplying my office with documentation that he has collected, and I plan to review and discuss these issues with Associate Counsel Therese Flynn-Eckford in order to determine how best to proceed.

PLS. 5014 01 April 2014

Exhibit 19



From: Colleen Struss [mailto:cstruss@aaas.org] Sent: Thursday, September 18, 2014 1:58 PM To: Eckford, Therese Flynn

Cc: Snyder, Peter; Monica Bradford; Paula Kiberstis

Subject: RE: Manuscript Request

Therese -

Thanks for your prompt response and confirmation of the employment relationship.

The manuscript you requested (our ID 1247422) is attached. This manuscript includes figures/images as part of the supplemental material.

Should you have any questions, please let me know. The file is fairly large, so I'd appreciate confirmation of receipt.

Sincerely,

Colleen Struss

Colleen Struss, JD, CPA

CFO/CLO
AAAS
1200 New York Avenue, NW
Washington, DC 20005
cstruss@anas.org
202-326-6691
MANAAS ANVANCING SCHROL STEVENG EQUIETY
CONFIDENTIALITY: This email and any attachments are privileged and confidential. If received in error, please do not disclose the contents to anyone, but notify the sender by return email and delete this email (and any attachments) from your system.
From: Eckford, Therese Flynn [mailto:Teckford@Lifespan.org] Sent: Thursday, September 18, 2014 11:26 AM To: Colleen Struss
Cc: Peter Snyder Subject: Re: Manuscript Request
Thank you Colleen. Dr. Medici was at the time of the submission and is currently an employee of Rhode Island Hospital, a hospital affiliate of Lifespan of which Lifespan is the sole member. appreciate your cooperation and please let me know if you have further questions.
Sincerely,
Therese Eckford

On Sep 18, 2014, at 11:10 AM, "Colleen Struss" < cstruss@aaas.org > wrote:

Dear Ms. Eckford,

Paula Kiberstis forwarded your request to me. As part of the scientific community, AAAS cooperates with investigations regarding scientific integrity. In my role as Chief Legal Officer, I need to ensure our response to your request is appropriate. I note the manuscript was submitted by Dr. Medici with an email address from Brown University. I understand Lifespan is affiliated with Brown, but could you confirm Dr. Medici was an employee of your institution at the time the manuscript was submitted? Once this is confirmed, I will forward the manuscript to you.

Sincerely,

Colleen Struss

Colleen Struss, JD, CPA

CFO/CLO

AAAS

1200 New York Avenue, NW

Washington, DC 20005

cstruss@aaas.org

202-326-6691

<image001.png>

CONFIDENTIALITY: This email and any attachments are privileged and confidential. If received in error, please do not disclose the contents to anyone, but notify the sender by return email and delete this email (and any attachments) from your system.

From: Eckford, Therese Flynn [mailto:Teckford@Lifespan.org]

Sent: Friday, September 12, 2014 10:42 AM

To: Paula Kiberstis **Cc:** Snyder, Peter

Subject: Manuscript Request

Dear Ms. Kiberstis:

I am writing to you in my capacity as in-house attorney and advisor to the Research Integrity Officer for the Lifespan Hospital System (Providence, Rhode Island), which includes Rhode Island Hospital. Unfortunately, we are currently investigating a research misconduct matter that involves a manuscript that was submitted to your journal for review sometime in the fall of 2013 (most likely in late September or early October). The manuscript was rejected from further consideration on November 22, 2013, pursuant to an e-mail letter from you. The manuscript was submitted by our employee Dr. Damian Medici, a co-author, and it appears from the correspondence I have seen that the submission number may have been #1247422. The manuscript is entitled: "Endothelial-Mesenchymal Transition Promotes the Natural Regression of Infantile Hemangioma" (Walsh et al.).

I am writing to ask whether you have archived the source files that were submitted to your journal (both the manuscript and accompanying figures), and, if so, whether you could please forward these files to us as they would be very useful to our internal investigation. Both I and Lifespan's Research Integrity Officer, Peter J. Snyder, Ph.D., would be very grateful if you could let us know whether these files can be provided.

Very truly yours,

Therese Eckford

Therese Flynn Eckford

Associate General Counsel

Lifespan Corporation

167 Point Street

Providence, RI 02903

(401) 444-3103 (phone)

(401) 444-6206 (fax)

EndMT Promotes the Natural Regression of Infantile Hemangiomas

Logan A. Walsh,¹⁻³ Diana Ramirez,⁴⁻⁷ Melissa Ramirez,⁴⁻⁷ John B. Mulliken,⁸ Damian Medici^{1,2,4-7*}

¹Division of Matrix Biology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02115, USA.

²Department of Developmental Biology, Harvard School of Dental Medicine, Harvard Medical School, Boston, MA 02115, USA.

³Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, USA.

⁴Department of Orthopaedics, Warren Alpert Medical School of Brown University, Providence, RI 02903, USA.

⁵Division of Hematology/Oncology, Department of Medicine, Warren Alpert Medical School of Brown University, Providence, RI 02903, USA.

⁶Laboratory for Regenerative Medicine, Rhode Island Hospital, Providence, RI 02903, USA.

⁷Cardiovascular Research Center, Rhode Island Hospital, Providence, RI 02903, USA.

⁸Department of Plastic and Oral Surgery, Boston Children's Hospital, Harvard Medical School, Boston, MA 02115, USA.

*Corresponding author: damian medici@brown.edu

Abstract:

Ilemangiomas are the most common tumors of infancy and arise by clonal expansion of vascular endothelial cells. These tumors rapidly proliferate during the first year of life then undergo a slow regression and disappear before adolescence. Adipogenesis is a hallmark of hemangioma regression, as the endothelial tumor is replaced by fat tissue over time. Here we show that endothelial-mesenchymal transition (EndMT) is a critical mechanism of hemangioma regression that mediates the differentiation of hemangioma endothelial cells into adipocytes. We show that the adipocytes in regressing hemangiomas express endothelial biomarkers. X-chromosome inactivation studies demonstrate that these adipocytes are clonal, suggesting that they are derived from the endothelial tumor cells. Macrophages infiltrate the tumors in the regressing phase and promote EndMT by secreting transforming growth factor-beta2 (TGF-β2). Insulin-like growth factor-1 (IGF-1), also secreted by macrophages and systemically elevated with age in response to human growth hormone, is essential for differentiating these endothelial-derived mesenchymal cells into adipocytes. These data identify a critical role for EndMT-dependent differentiation of vascular endothelial cells into fat cells during hemangioma regression and provide evidence that EndMT can resolve human disease.

One Sentence Summary:

Endothelial cells transform into adipocytes to mediate hemangioma regression.

Main Text:

Infantile hemangiomas are vascular tumors that occur in approximately 10% of Caucasian infants (1-4). Most are cutaneous and occur within the head and neck region (5). Hemangiomas arise by hyperactive vascular endothelial growth factor (VEGF) signaling (6, 7). Heterozygous germ-line mutations in hemangioma endothelial cells (HemECs) prevent expression of the VEGF receptor 1 (VEGFR1), a decoy receptor that sequesters VEGF and prevents it from binding to VEGFR2. This allows VEGF to constitutively activate VEGFR2 and induce endothelial proliferation (8). Although the mechanisms that cause proliferation of hemangiomas have been discovered, little is known about how these tumors naturally regress. The predominant event that occurs during hemangioma regression is adipogenesis, as the endothelial tumor is replaced by fat tissue over time (3).

We previously reported that endothelial-mesenchymal transition (EndMT), a prominent mechanism of embryonic development (9) and fibrosis (10-12), represents a reversion to a mesenchymal stem cell phenotype with multipotent differentiation capabilities (13, 14). This endothelial differentiation occurs in a rare disorder called fibrodysplasia ossificans progressiva, in which patients exhibit massive heterotopic ossification of their soft tissues (13, 15). Combined with inflammation, a heterozygous germ-line mutation in a TGF-β/BMP receptor called ALK2 triggers EndMT and subsequent differentiation into chondrocytes and osteoblasts, which produce heterotopic bone (13). Based on these studies, we hypothesized that EndMT might occur during hemangioma regression to mediate the differentiation of the endothelial tumor cells into adipocytes.

Tissue sections from six independent regressing hemangiomas were analyzed by immunohistochemistry using antibodies specific for the adipocyte marker adiponectin and

endothelial markers TIE2, vWF, and VE-cadherin. Adipocytes in regressing hemangiomas stained positive for endothelial markers, whereas adipocytes from six normal subcutaneous adipose tissue specimens showed no expression of endothelial markers (Fig. 1A). Quantification of adipocyte populations from regressing hemangiomas showed that approximately 60% of the adipocytes expressed endothelial markers (Fig. 1B).

Currently, there is no genetic mouse model of infantile hemangioma, otherwise lineage tracing could be performed in order to confirm the endothelial origin of the adipocytes. However, there is another method for tracing whether the adipocytes are derived from HemECs. X-chromosome inactivation studies, used to distinguish cancer cells from non-cancer cells (16), have shown that HemECs are clonal (17). Therefore, if the adipocytes in regressing hemangiomas are formed from the HemECs, they should also be clonal.

Adipocytes from regressing hemangiomas were isolated by enzymatic dissociation of the tissues to acquire cells in suspension then stained using antibodies specific for the adipocyte marker adiponectin and endothelial marker VE-cadherin. Cells expressing adiponectin and VE-cadherin, or adiponectin alone, were isolated by fluorescence-activated cell sorting (FACS). DNA was extracted from these two populations of adipocytes and X-chromosome inactivation studies were performed to assess clonality by methylation of the human androgen receptor (HUMARA) gene. Using a restriction enzyme (Hhal) that targets a methylation site of this gene, we performed methylation-specific PCR to determine whether one of the HUMARA alleles was silenced. Based on analysis of amplified DNA from subpopulations of adipocytes isolated from regressing hemangiomas, we determined that adipocytes that do not express the endothelial marker VE-cadherin are not clonal. Adipocytes that express VE-cadherin demonstrated allele silencing and are therefore clonal, suggesting they are derived from HemECs (Fig. 1C).

To determine whether this endothelial differentiation to adipocytes could be caused by EndMT, tissue sections from six different proliferating hemangiomas and six regressing hemangiomas were stained with antibodies specific for the mesenchymal marker FSP-1 and the endothelial markers TIE2, vWF, or VE-cadherin. Proliferating hemangiomas showed little or no co-expression of endothelial and mesenchymal markers by immunofluorescence, while regressing hemangiomas had intense co-expression of these markers (Fig. 2, A and B).

To trace whether mesenchymal cells expressing endothelial markers in regressing hemangiomas are derived from HemECs, we performed X-chromosome inactivation studies to determine clonality of these cells. Regressing hemangioma tissues were dissociated and sorted by FACS to identify cells expressing the mesenchymal marker FSP-1 and endothelial marker VE-cadherin from those that only express FSP-1. DNA was extracted from these subpopulations, followed by methylation-specific PCR to determine clonality. We observed allele silencing of the *HUMARA* gene in the populations of mesenchymal cells expressing VE-cadherin, but not in those lacking VE-cadherin expression (Fig. 2C). These data suggest that EndMT of HemECs occurs during hemangioma regression.

By analyzing cellular populations of hemangioma tissues with flow cytometry, we found that regressing hemangiomas contained higher numbers of macrophages than proliferating hemangiomas by assessing expression of macrophage marker EMR-1, the human homolog of F4/80 (Fig. 3A). The most common factor known to induce EndMT is TGF- β 2 (13, 14, 18, 19), an inflammatory cytokine produced by macrophages (20). Immunoblotting of tissue lysates showed higher expression of TGF- β 2 in regressing hemangiomas compared to proliferating hemangiomas (Fig. 3B). Macrophages from regressing hemangiomas were isolated into primary culture by FACS and protein levels of TGF- β 2 in these cells were analyzed by immunoblotting.

Hemangioma macrophages (HemMPs) showed high expression of TGF-β2, whereas HemECs showed very little expression (Fig. 3C). ELISA demonstrated high levels of secreted TGF-β2 in the conditioned medium collected from HemMPs compared to HemECs (Fig. 3D).

To determine the effects of HemMPs on HemECs, we collected conditioned medium from cultured HemMPs and exposed HemECs to this medium. We observed a dramatic change in cell morphology characteristic of EndMT within 24 hours. Control cells exposed to serum-free medium maintained the cobblestone-like endothelial morphology (Fig. 3E). We also noted reduced expression of the endothelial marker CD31 and increased expression of mesenchymal markers FSP-1 and α-SMA in HemECs exposed to HemMP conditioned medium (Fig. 3F). Mixing HemMP conditioned medium with neutralizing antibodies specific for TGF-β2 was sufficient to inhibit EndMT, suggesting that macrophages induce EndMT in a TGF-β2-dependent manner (Fig. 3, E and F).

Recombinant TGF-β2 has been shown to induce EndMT in normal vascular endothelial cells (13, 14, 19), so we attempted to determine whether this would occur with HemECs. Surprisingly, recombinant TGF-β2 alone was insufficient to induce EndMT (fig. S1, A and B). This is likely due to the constitutive VEGF signaling in HemECs that promotes their proliferation and tumor formation (6, 8). VEGF is a known inhibitor of EndMT (13, 21). We previously reported that restoring soluble VEGFR1 (sVEGFR1) levels can inhibit VEGF signaling and proliferation of HemECs (8). Treating HemECs with a combination of TGF-β2 and sVEGFR1 for 48 hours was sufficient to induce EndMT, as shown by changes in cell morphology and in expression of EndMT markers (fig. S1, A and B). Protein levels of sVEGFR1 were analyzed in tissue lysates of proliferating and regressing hemangiomas showing that the regressing tumors contained substantially more sVEGFR1 (fig. S1C). Macrophages have been

reported to express sVEGFR1 (22), so we analyzed lysates and conditioned medium from HemMPs to determine the levels of expression. HemMPs showed high levels of sVEGFR1 expression, but HemECs did not (fig. s1, D and E). These data suggest that the combined secretion of TGF-β2 and sVEGFR1 from infiltrating macrophages stimulates EndMT in regressing hemangiomas.

Cells that undergo EndMT have been shown to acquire properties of stem cells (13, 14). We confirmed this in HemECs by immunoblotting for mesenchymal stem cell markers STRO-1, CD44, and CD90, as well as assessing adipogenic potential by Oil red O staining. HemECs exposed to TGF-β2 and sVEGFR1 for 48 hours to induce EndMT showed high expression of these mesenchymal stem cell markers (fig. S2A). These HemEC-derived mesenchymal stem-like cells were successfully converted into adipocytes after exposure to adipogenic culture medium for 9 days (fig. S2B).

The most common factors that induce stem cell differentiation to adipocytes are insulin and insulin-like growth factors (23). Insulin-like growth factor-1 (IGF-1) is an inflammatory cytokine produced by macrophages (24). Analysis of IGF-1 levels in proliferating and regressing hemangioma lysates showed more IGF-1 expression in the regressing tissues (Fig. 4A). We analyzed IGF-1 expression by immunoblotting and IGF-1 secretion by ELISA in HemMPs compared to HemECs and found that the endothelial cells produce little or no IGF-1, whereas the macrophages produce high levels of IGF-1 (Fig. 4, B and C). To determine the adipogenic potential of IGF-1 on HemECs that have undergone EndMT, the endothelial cells pre-treated with sVEGFR1 were exposed to TGF-β2 for 48 hours to induce EndMT, followed by 9 days of treatment with recombinant IGF-1. Oil red O staining confirmed formation of adipocytes in these

cultures. Treatment of HemECs with TGF-β2 or IGF-1 alone did not produce adipocytes (Fig. 4D).

All three cytokines (sVEGFR1, TGF- β 2, and IGF-1) necessary for EndMT and adipogenic differentiation of HemECs are produced by macrophages. Therefore, we hypothesized that HemMP conditioned medium alone would be sufficient to induce adipocyte formation from HemECs. While macrophage conditioned medium stimulated EndMT (Fig. 3, E and F), we did not observe adipocyte formation by Oil red O staining (Fig. 4E). A recent study has shown that macrophages inhibit adipogenesis by producing the potent anti-adipogenic cytokine IL-1 β (25). We tested whether this was the case with HemMPs by mixing IL-1 β neutralizing antibodies with the macrophage conditioned medium. Exposure of HemECs to this medium caused adipocyte formation within 9 days of treatment (Fig. 4E).

Studies have shown that exposing macrophages to human growth hormone (hGH) can switch them from anti-adipogenic to adipogenic behavior by inhibiting their production of IL-1β (25). Since hGH is systemically at its highest levels in childhood (26), and all patients with infantile hemangioma are children, we hypothesized that hGH could have a role in promoting the adipogenic effects of HemMPs by inhibiting IL-1β expression. We treated HemMPs with hGH for 8 hours in culture to assess possible effects on IL-1β and IGF-1 expression. hGH dramatically reduced IL-1β expression and increased IGF-1 expression in HemMPs (Fig. 4F). We exposed HemECs to conditioned medium from HemMPs that were pre-treated with hGH and observed formation of adipocytes within 9 days. This occurs in an IGF-1-dependent manner, as mixing IGF-1 neutralizing antibodies with the conditioned medium from HemMPs pre-treated with hGH blocked adipogenesis (Fig. 4G).

Blood samples were collected from six individuals with proliferating hemangiomas and six with regressing hemangiomas. ELISA analysis of serum from these specimens showed that on average those with regressing hemangioma (age 1-10 years) had higher hGH levels than those with proliferating hemangioma (less than 1 year of age), although these levels are within the normal range for children of this age (26) (Fig. 4H). Also, since hGH is circadian and released from the pituitary gland at different times (27), it is more important to assess an hGH target rather than the hormone itself. The primary function of hGH is to act on liver cells to promote the production of IGF-1, which stimulates tissue growth (23). IGF-1 also promotes stem cell differentiation to adipocytes (27) and is locally produced by macrophages at high levels in regressing hemangiomas (Fig. 3). To assess systemic levels of IGF-1 we analyzed blood serum from hemangioma patients by ELISA. We found that individuals with regressing hemangiomas had much higher systemic IGF-1 than those with proliferating hemangioma (Fig. 41).

Our data suggest a two-fold effect of hGH in regulating hemangioma regression. First, hGH locally affects macrophages in hemangioma tumors by inhibiting their production of IL-1β and increasing IGF-1 expression. Second, hGH systemically increases IGF-1 levels produced by the liver, which are higher during the regressing phase of the disease. Our data suggest that elevated IGF-1 levels contribute to endothelial-derived mesenchymal cells differentiating into adipocytes to mediate hemangioma regression (fig. S3).

Although most of the adipocytes in regressing hemangiomas arise from the HemECs, a significant population of non-clonal adipocytes appears as well. It is unclear as to what other cell types might produce these non-clonal adipocytes. A small population of resident hemangioma stem cells has been reported to have been isolated from the proliferating tumors and have shown the ability to undergo adipogenesis (3, 28, 29). Other candidates include stem or progenitor cells

recruited from bone marrow or surrounding tissues, or pericytes, which are mesenchymal cells described to have stem cell-like properties (30).

By replicating the mechanisms of hemangioma regression, the conversion of endothelial cells into fat cells may provide a novel therapeutic treatment for hemangiomas and other vascular or angiogenesis-dependent tumors.

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Acknowledgements:

We thank J. Bischoff (Boston Children's Hospital), B. Olsen (Harvard Medical School), R. Kalluri (M.D. Anderson Cancer Center), H. Taylor (Rhode Island Hospital), and S. Sullivan (Rhode Island Hospital) for providing materials for this study. This work was supported by grants R01HL112860 and P20GM104937 from the National Institutes of Health (to D.M.) and a grant from the John Butler Mulliken Foundation (to D.M.).

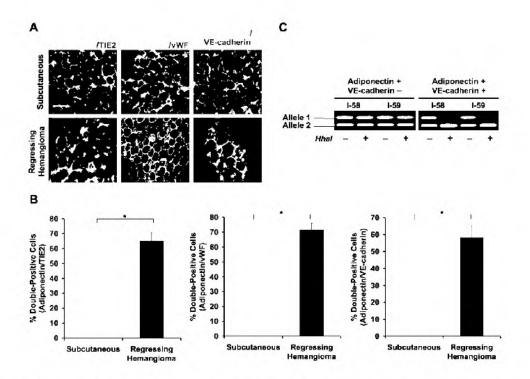


Fig. 1. Hemangioma endothelial cells transform into adipocytes in regressing hemangiomas. (A) Immunohistochemistry showing expression of endothelial markers TIE2, vWF and VE-cadherin in adipocytes from regressing hemangioma tissue, but no expression of endothelial markers was observed in normal subcutaneous adipocytes. Scale bar, 10 μ m. (B) Quantification of immunohistochemical analyses. (C) X-chromosome inactivation analysis by methylation-specific PCR showing clonality of adipocytes isolated from regressing hemangiomas (I-58, I-59) that express endothelial marker VE-cadherin by allele silencing of the HUMARA gene. Adipocytes not expressing VE-cadherin were not clonal. Graphs represent mean (n=6) \pm SD; *P<0.001 by Student's t test.

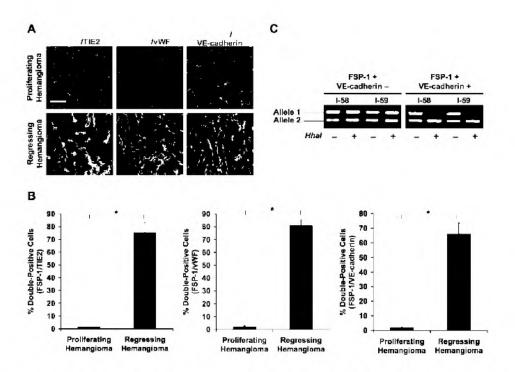


Fig. 2. Endothelial-mesenchymal transition occurs during hemangioma regression. (A) Immunohistochemistry showing co-expression of endothelial markers TIE2, vWF and VE-cadherin with mesenchymal marker FSP-1 in regressing hemangiomas. Proliferating hemangiomas showed little or no co-expression. Scale bar, 10 μ m. (B) Quantification of immunohistochemical analyses. (C) X-chromosome inactivation analysis by methylation-specific PCR showing clonality of mesenchymal cells in regressing hemangiomas (I-58, I-59) that express endothelial marker VE-cadherin by allele silencing of the *HUMARA* gene. Mesenchymal cells lacking VE-cadherin expression were not clonal. Graphs represent mean (n=6) \pm SD; *P<0.01 by Student's t test.

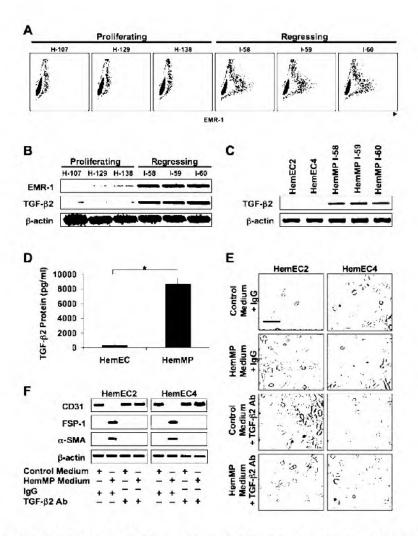


Fig. 3. Macrophages induce EndMT in regressing hemangiomas in a TGF-β2-dependent manner. (A) Flow cytometry analysis of quantity of macrophages in proliferating (H-107, H-129, H-138) and regressing (I-58, I-59, I-60) hemangiomas by EMR1 (F4/80) expression. (B) Immunoblotting showing higher expression of EMR1 and TGF-β2 in regressing hemangioma tissue compared to proliferating hemangioma tissue. (C) Immunoblotting showing little or no expression of TGF-β2 in hemangioma endothelial cells (HemEC2, HemEC4) and high expression of TGF-β2 in hemangioma macrophages (HemMP) isolated from regressing hemangiomas. (D) ELISA analysis of secreted TGF-β2 levels in conditioned medium from primary HemECs and HemMPs. (E) DIC imaging of HemECs exposed to serum-free control medium or HemMP conditioned medium (HemMP Medium) in the presence of a non-specific IgG control or to TGF-β2 neutralizing antibodies (TGF-β2 Ab) showing that HemMP conditioned medium induces EndMT, which is inhibited by TGF-β2 neutralizing antibodies. Scale bar, 20 µm. (F) Immunoblotting showing decreased expression of endothelial marker CD31 and increased expression of mesenchymal markers FSP-1 and α-SMA after exposure of HemECs to HemMP conditioned medium. TGF-\(\beta\)2 neutralizing antibodies block these changes. Data represent mean (n=6) \pm SD; *P<0.01 by Student's t test.

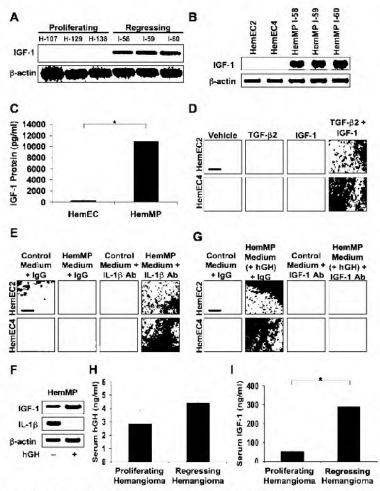


Fig. 4. Human growth hormone (hGH) promotes adipogenic differentiation of hemangioma endothelial cells after EndMT by inhibiting IL-1β and inducing IGF-1 expression. (A) Immunoblotting showing that regressing hemangioma (I-58, I-59, I-60) tissues have higher expression of IGF-1 than proliferating hemangioma (H-107, H-129, H138). (B) Immunoblotting showing that hemangioma macrophages (HemMP) highly express IGF-1, whereas hemangioma endothelial cells (HemEC) do not. (C) ELISA analysis of secreted IGF-1 in conditioned medium from primary HemECs and HemMPs. (D) Oil red O staining showing that treatment of HemECs (pre-treated with sVEGFR1) with TGF-β2 followed by IGF-1 promotes adipogenesis. (E) Oil red O staining showing that HemMP conditioned medium failed to induce adipocyte formation from HemECs, but presence of IL-16 neutralizing antibodies permitted adipocyte formation by HemMP conditioned medium. (F) Immunoblotting showing increased IGF-1 expression and decreased IL-1\(\text{g}\) expression in HemMPs treated with human growth hormone (hGH). (G) Oil red O staining showing formation of adipocytes after HemECs were exposed to HemMP conditioned medium from macrophages pre-treated with hGH. Presence of IGF-1 neutralizing antibodies blocked adipocyte formation. (H and I) ELISA analysis of hGH (H) and IGF-1 (I) in blood serum from patients with proliferating hemangiomas and regressing hemangiomas showing higher levels during the regressing phase. Graphs represent mean (n=6) \pm SD; *P<0.05 by Student's t test. Scale bars, 50 µm.

Supplementary Materials for

EndMT Promotes the Natural Regression of Infantile Hemangiomas

Logan A. Walsh, Diana Ramirez, Melissa Ramirez, John B. Mulliken, Damian Medici*

*Corresponding author. Email: damian_medici@brown.edu

Materials and Methods Fig. S1-S3

Materials and Methods

Human Tissues. All patient samples were obtained with informed consent and protocols approved by the Investigational Review Boards of the Boston Children's Hospital, Harvard Medical School, and Rhode Island Hospital. All tissues used were those that would normally be discarded after surgeries. Blood samples were acquired during essential surgeries with informed consent. All specimens were de-identified and assigned a number before being used for this study. These include proliferating hemangioma tissues (H-29, H-64, H-73, H-107, H-129, H-138), regressing hemangioma tissues (I-58, I-59, I-60, I-69, I-78, I-85), subcutaneous adipose tissues (SA-1, SA-2, SA-3, SA-4, SA-5, SA-6), isolated primary hemangioma endothelial cells (HemEC1, HemEC2, HemEC4, HemEC17B, HemEC21A, HemEC24), blood from individuals with proliferating hemangiomas (H-149, H-150, H-151, H-154, H-155, H-156) and blood from individuals with regressing hemangiomas (I-72, I-74, I-75, I-76, I-78, I-85). The investigation conformed to the principles outlined in the Declaration of Helsinki.

Cell culture. Primary human hemangioma endothelial cells were provided by Dr. Joyce Bischoff (Boston Children's Hospital) and isolated as previously described (17). Endothelial cells were grown in culture using EGM-2 medium (Lonza), containing 20% FBS and 1% Penicillin/Streptomycin, followed by human endothelial serum free medium (Gibco) 24 hours prior to all experimental conditions. Hemangioma macrophages isolated from regressing hemangioma tissues were grown in RPMI 1640 medium (Gibco) containing 10% FBS and 1% Penicillin/Streptomycin, followed by macrophage serum-free medium (Gibco) 24 hours prior to all experimental conditions. Recombinant TGF-β2, IGF-1, and sVEGFR1 (R&D Systems) were added to the serum-free culture medium at a concentration of 10 ng/ml. Neutralizing antibodies specific for TGF-β2 (ab10850; Abcam), IGF-1 (AF-291-NA) and IL-1β (MAB601; R&D Systems) were added to the medium at a concentration of 1 μg/ml each. The StemPro Adipogenesis Differentiation Kit (Life Technologies) was used to test adipogenic potential of HemECs for nine days after treatment with EndMT-inducing stimuli. All experiments for this study were performed at minimum in triplicate.

Immunohistochemistry. Tissues were frozen in OCT compound (Tissue-Tek) and sectioned onto glass slides using a HM550 cryostat sectioner (Thermo Scientific). Tissues were permeablized with cold acetone for 15 minutes then washed with PBS and blocked with 10% FBS mixed into a solution of 1% BSA for 1 hour at room temperature. Antibodies specific for TIE2 (sc-324; Santa Cruz Biotechnology), vWF (ab154193), VE-cadherin (ab33168), adiponectin (ab22554; Abcam), and FSP-1 (H00006275-M01; Abnova) were used at a dilution of 1:50 in a solution of 1% BSA for 2 hours at room temperature. Tissues were then washed three times with PBS for 5 minutes each. AlexaFluor 488 IgG and AlexaFluor 594 IgG secondary antibodies (Invitrogen) were used at a dilution of 1:200 in a solution of 1% BSA for 2 hours at room temperature. Tissues were washed three times with PBS for 5 minutes each and allowed to dry completely. Vectashield (Vector Labs) fluorescent mounting medium was used to attach the cover slips to glass slides. Images were captured using a Nikon 80i fluorescent microscope.

Immunoblotting. Cell lysates were collected using RIPA buffer (Pierce) supplemented with Halt protease and phosphatase inhibitor cocktail (Pierce). Protein (20 µg) was resolved by SDS-

PAGE, transferred onto immobilon-P-membranes (Millipore), and blocked with 5% dry milk in TBS-T (TBS [pH7.6], 0.1% tween20). Primary antibodies specific for CD31 (IR610; Dako), FSP-1 (H00006275-M01; Abnova), EMR1 (HM1066; Hycult Biotech), TGF-β2 (MAB612), IGF-1 (AF-291-NA), IL-1β (MAB601; R&D Systems), STRO-1 (sc-47733), CD44 (sc-71220), CD90 (sc-9163; Santa Cruz Biotechnology), sVEGFR1 (36-1100; Life Technologies), α-SMA (A5228), and β-actin (A1978; Sigma-Aldrich) were used at a dilution of 1:1000. HRP-conjugated IgG TrueBlot secondary antibodies (eBioscience) were used at a dilution of 1:1000. Protein bands were visualized using an enhanced chemiluminescence detection system (Pierce). Membranes were stripped for reprobing using Restore Western Blot Stripping Buffer (Pierce).

Clonality assays. X-chromosome inactivation HUMARA assays were performed as previously described (17). DNA was isolated using the DNA Mini kit and protocol (Qiagen). 5 µg of DNA from each sample was digested with 20 units of *Hhal* restriction enzyme (New England Biolabs) or no enzyme as a control and incubated at 37°C for 24 hours. 1 µl of each sample was used for PCR. The following primers were used: 5'-GCTGTGAAGGTTGCTGTTCCTCAT-3' and 5'-TCCAGAATCTGTTCCAGAGCGTGC-3' at a 20 nM concentration. The reactions contained 0.5 units of Taq DNA Polymerase, 0.5 µl dATP, 10X buffer, and 15 mM MgCl₂ (Qiagen). The cycling steps were as follows: Initial denaturing at 92°C for 3 minutes, 30 cycles of denaturing at 92°C for 40 seconds, annealing at 65°C for 40 seconds, extension at 72°C for 40 seconds, final extension at 72°C for five minutes. Samples were run on 1.5% agarose gels stained with ethidium bromide. Gels were imaged using a Molecular Imager gel doc (Bio-Rad).

Flow cytometry. Regressing hemangioma specimens were enzymatically digested using collagenase and dispase (Sigma-Aldrich) according to the manufacturer's protocol and dissociated using the gentleMACS tissue dissociator (Miltenyi Biotech). Cells were stained in suspension using antibodies specific for adiponectin (ab22554), VE-cadherin (ab33168; Abcam), EMR1 (HM1066; Hycult Biotech) or FSP-1 (H00006275-M01; Abnova) at a 1:50 dilution, followed by AlexaFluor 488 IgG and AlexaFluor 594 IgG secondary antibodies at a 1:200 dilution. Flow cytometry/cell sorting was performed at the Harvard Medical School Department of Pathology flow cytometry core facility using a FACSAria (BD Biosciences) cell sorter. Data were analyzed using WinMDI software.

ELISA. Lysates of HemECs and HemMPs or blood serum specimens were analyzed using the Quantikine Human TGF-β2 Immunoassay kit, Quantikine Human IGF-1 Immunoassay kit, Quantikine Human hGH Immunoassay kit, or Quantikine Human sVEGF-R1/Flt-1 Immunoassay kit (R&D Systems) following the manufacturer's protocols. Samples were analyzed for optical density using an iMark microplate reader (Bio-Rad).

Oil red O staining. To detect adipocytes, cell cultures were stained with Oil Red O (Sigma-Aldrich) for 15 minutes and washed 3 times with PBS for 5 minutes each, followed by observation under a Nikon SMZ445 dissecting microscope.

Statistics. One-way analysis of variance (Λ NOV Λ) and/or two-tailed paired student's t test were performed using GraphPad Prism 5 software. P values less than 0.05 were considered significant.

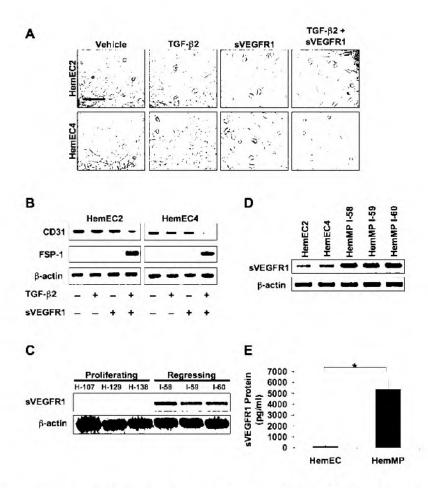


Fig. S1. TGF-β2 stimulates EndMT of hemangioma endothelial cells when VEGF signaling is inhibited. (A) DIC imaging showing that TGF-β2 alone was insufficient to induce EndMT of hemangioma endothelial cells (HemEC), but a combination of TGF-β2 and sVEGFR1 permits EndMT. Scale bar, 20 μm. (B) Immunoblotting showing that TGF-β2 and sVEGFR1 promote decreased expression of the endothelial marker CD31 and increased expression of the mesenchymal marker FSP-1. (C) Immunoblotting showing that regressing hemangiomas (I-58, I-59, I-60) have higher expression of sVEGFR1 than proliferating hemangiomas (H-107, H-129, H138). (D) Immunblotting showing that HemECs express little sVEGFR1, whereas hemangioma macrophages (HemMP) produce high amounts of sVEGFR1. (E) ELISA analysis of secreted sVEGFR1 from HemMPs compared to HemECs. Data represent mean (n=6) ± SD; *P<0.01 by Student's t test.

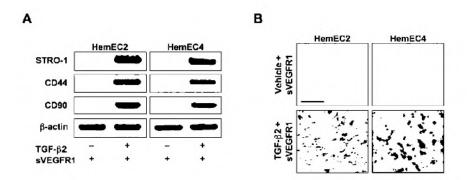


Fig. S2. HemECs that undergo EndMT acquire properties of mesenchymal stem cells with adipogenic potential. (A) Immunoblotting showing that HemECs treated with TGF- β 2 and sVEGFR1 express mesenchymal stem cell markers STRO-1, CD44, and CD90. (B) Oil red O staining showing adipocyte formation in HemEC cultures treated with TGF- β 2 and sVEGFR1 for two days, followed by nine days of exposure to adipogenic culture medium. Scale bar, 50 μ m.

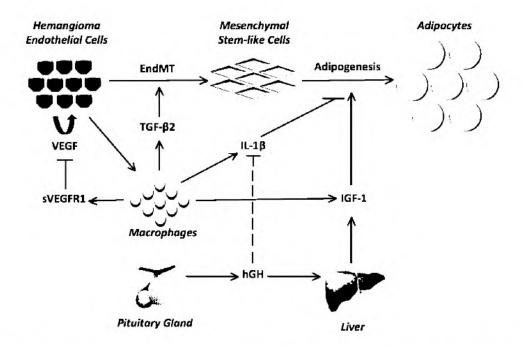


Fig. S3. A schematic diagram of the proposed mechanism of hemangioma regression. Hemangiomas arise by constitutive VEGF signaling. Macrophages infiltrate the tumor over time and secrete sVEGFR1, which binds and sequesters VEGF to inhibit proliferation. This inactivation of VEGF also allows EndMT induction by TGF-β2 secreted from macrophages. These newly formed mesenchymal stem-like cells are differentiated into adipocytes by IGF-1 that is produced by the infiltrating macrophages, but can also be blocked by IL-1β. Since patients with infantile hemangioma are children with systemically high levels of hGH, IL-1β production from macrophages is inhibited by the hormone. Also, hGH primarily targets the liver to induce production of the adipogenic cytokine IGF-1, suggesting that systemic hGH may have a two-fold effect on mediating hemangioma regression.

Subject:Re: Paper update

Date:Fri, 27 Sep 2013 10:06:07 -0400

From: Medici, Damian < damian medici@brown.edu>

To:Mulliken, John < John.Mulliken@childrens.harvard.edu>

Yes, we'll likely try endostatin too. There are several drugs we would like to try to test to determine whether they will inhibit the proliferation or speed up the involution, but it all depends on availability of specimens. Propranolol works so well that it's difficult to get proliferating hemangioma specimens anymore. Fortunately, Helena gave us a good size tumor which we cut into 16 pieces and implanted in mice. Since we previously found that the tumors arise by hyperactive VEGF signaling, we figured Avastin would be the logical choice as our first drug to test. I'll keep you updated on our findings.

Best,

Damian

On Fri, Sep 27, 2013 at 8:59 AM, Mulliken, John < <u>John, Mulliken@childrens.harvard.edu</u>> wrote:

Damian,

Remember Boye E, et al., 2001, Endostatin stimulated HemEC migration.

John

From: Medici, Damian [mailto:damian medici@brown.edu]

Sent: Thursday, September 26, 2013 11:19 PM

To: Mulliken, John

Subject: Re: Paper update

Sounds good. I'll reformat it and submit sometime next week. You'll probably get a confirmation of submission email from Science, which I believe they send to all of the authors.

I also thought you might like to know that we are currently testing Avastin in our mice with hemangioma implants. We should have the results in a few weeks.

Best,
Damian
On Thu, Sep 26, 2013 at 5:21 PM, Mulliken, John < <u>John Mulliken@childrens.harvard.edu</u> > wrote:
Damian,
You have my enthusiastic approval to pull the MS from Nature Med.and send to Science.
John
From: Medici, Damian [mailto:damian medici@brown.edu] Sent: Thursday, September 26, 2013 2:57 PM To: Mulliken, John Subject: Paper update
Hi John,
Our paper on hemangioma involution that we sent to Nature Medicine has been taking an extremely long time. They did an initial internal review by the editorial board. We did the
revision that they requested and sent it back so they would send it for external peer review. We have been waiting over 4 months for that, but still no reviews. The editor requested additional

information in the form of an 18 question checklist, which needs to be filled out and sent back to him and will now delay things further. We have become so frustrated with them that I have been

looking for other options.

I contacted an editor I know at Science magazine to inquire whether she would be interested and she said that she is very interested and would immediately send it for external review if we submit it to Science. I've spoken to the other authors and we are all in agreement that we should withdraw the paper from Nature Medicine and submit it to Science. Science is a much better journal than Nature Medicine, so I think we have a golden opportunity here to publish in one of the most elite journals. Since you are an author, I need your approval as well, so please let me know if you are OK with this.

Best,
Damian
Damian Medici, Ph.D.
Assistant Professor of Orthopaedics and Medicine
Warren Alpert Medical School of Brown University
Director, Laboratory for Regenerative Medicine
Rhode Island Hospital
1 Hoppin Street, Coro West, Suite 402C
Providence, RI 02903
Tel: <u>401-444-7180</u>
Fax: <u>401-444-5006</u>
Email: damian_medici@brown.edu
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Subject:Re: Cell Stem Cell Editorial Decision for CELL-STEM-CELL-D-14-00111 Date:Mon. 17 Feb 2014 16:21:42 -0500 From:Medici, Damian <damian medici@brown.edu> To:Logan Walsh < walshl@mskcc.org> Just busy all the time. Stressing out about wedding stuff too (as expected). Yeah man, I have today off so give me a call whenever you're free so we can catch up. D On Mon, Feb 17, 2014 at 3:17 PM, <walshl@mskcc.org> wrote: Awesome..... How are you otherwise? Wanna chat later? From: Medici, Damian [mailto:damian_medici@brown.edu]

Sent: Monday, February 17, 2014 3:15 PM To: Walsh, Logan A./Sloan-Kettering Institute

Subject: Fwd: Cell Stem Cell Editorial Decision for CELL-STEM-CELL-D-14-00111

----- Forwarded message ------

From: Cell Stem Cell Editorial <stemcell@cell.com>

Date: Mon, Feb 17, 2014 at 1:34 PM

Subject: Cell Stem Cell Editorial Decision for CELL-STEM-CELL-D-14-00111

To: Damian Medici < damian medici@brown.edu>

Dr. Damian Medici **Brown University** 1 Hoppin Street Coro West 402C Providence, RI 02903 UNITED STATES

Feb 17, 2014

RE: CELL-STEM-CELL-D-14-00111

"Endothelial-Mesenchymal Transition Promotes the Natural Regression of Infantile Hemangioma"

Dear Dr. Medici,

Thank you for submitting your paper to Cell Stem Cell. I have read your manuscript with interest and discussed it with the editorial team. I appreciate that in this study you characterize the progression of how hemangiomas regress in patient derived samples. To this end, I appreciate that you find, using X-inactivation analysis, that adipocytes in the hemangiomas are clonal, indicating that they are derived from the endothelial cells via endothelial-mesenchymal transition. You also find that macrophages are present at higher numbers in regressing samples, and present data suggesting that TGFbeta and IGF1 secreted by infiltrating cells drive the cellular conversion process. Although the study appears to be well executed overall, and the work on the human samples has merit, I was not sure about the broader interest of these findings beyond the immediate field. I therefore sought informal advice on the paper from an expert in the field and have now heard back from him/her.

Although he/she commented positively on the work being quite nice, and would make a nice contribution to the existing literature on this topic, he/she felt the paper with its current scope would not be likely to fare well in review here. He/she commented that infantile hemangiomas are benign and self-resolve, and that the clinical importance of the findings therefore remains limited. He/she also felt that for a stem cell audience, stronger functional data pointing to how these mechanisms may be operable in driving endothelial-mesenchymal transitions in more aggressive tumors would be required. Based on this consideration, I would like to suggest that publication would be more appropriate in another journal.

This decision does not involve any criticism of your data, but simply reflects the scope of Cell Stem Cell and the intense pressure for space in the journal. These constraints make it impossible for us to publish all the submitted papers that are of high quality and interest in the field they represent. The number of submissions is several times greater than the number of papers that could be published, so we are compelled to make a preliminary selection of manuscripts at the stage of submission, before review. When it seems that a paper does not fit our editorial criteria, we try to avoid unnecessary delays by returning the manuscript without a detailed review. We believe that in such cases it is in the best interest of the author to indicate immediately that there is a high probability that reviewers would recommend against publication in Cell Stem Cell.

However, I hope that you will feel free to submit other papers to Cell Stem Cell in the future when it seems appropriate. For this particular paper, you may want to consider submitting to our newest journal, Cell Reports.

Yours sincerely,

Christina Lilliehook, Ph.D., Ph.D. Scientific Editor, Cell Stem Cell

The EM is at http://cell-stem-cell.edmgr.com/

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error, please notify the sender immediately by replying to this message
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From: Snyder, Peter <psnyder@Lifespan.org>
To: browngradstudent1@yahoo.com

CC: Snyder, Peter

Sent: 4/1/2014 2:06:05 PM

Subject: Confidential Update - and a request

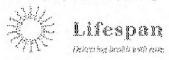
Hi Michael, I discussed this issue today with the General Counsel for the hospital system, and I am now working with one of his associates – a lawyer that specializes in research issues and management. I have worked with her many times before, and she is excellent. I am beginning to consider whom to choose for an 'inquiry committee', and once constituted, that committee will need to meet with you (per our discussion yesterday). Also, I will likely be able to keep this under the radar for about 3-4 weeks, but I may not be able to proceed much farther after that without Dr. Medici being made aware of the investigation. So, it will be very important for you to work with Assoc. Dean Harrington, and with your department chair, to consider alternate laboratories for you to work in over this next month. Again, I will help this along as much as possible – and I would be happy to talk with you about your interests beyond orthopedics and to try to find a good match for you.

I have one additional request for you at this time. I am sure that you have kept a "paper trail" of emails with Dr. Medici that are pertinent to your concerns. Since he did not use a Lifespan email address, I am unable to retrieve these. Could you please send to me (another Dropbox link would be perfect) ANY emails that you think that I, and the inquiry committee, need to read?? Please include all the header information for each email.

THANKS! Best wishes, Dr. Pete Snyder

Peter J. Snyder, Ph.D.
Sr. Vice President & Chief Research Officer,
Lifespan Hospital System, Providence, RI, U.S.A.
Professor of Neurology,
Alpert Medical School of Brown University
Sr. Associate Editor,
Alzheimer's & Dementia: The Journal of the Alzheimer's Association

Office Telephone: (401) 444-4117 E-Mail: psnyder@lifespan.org



From: Snyder, Peter <psnyder@Lifespan.org>

To: Brown Grad Student Sent: 4/2/2014 12:54:24 PM

Subject: RE: Confidential Update - and a request

Thanks Michael,

This most recent new is very disturbing. The inquiry committee will need to interview you, as well as the other lab members when the time comes. PLEASE gather any additional evidence....notes, photos, anything that can support your allegations – so that these can be properly considered by the committee. Thanks again, Dr. Pete Snyder

From: Brown Grad Student [mailto:browngradstudent1@yahoo.com]

Sent: Wednesday, April 02, 2014 12:26 PM

To: Snyder, Peter

Subject: Re: Confidential Update - and a request

Hi Dr. Snyder,

Please find attached the non-redacted e-mail that I mentioned in my previous e-mail to you.

In terms of unpublished papers, Jorna et al. is currently under review at BBRC (submitted 3/28/14). I do not know about the current status of the Walsh et al. paper because I'm not on that paper. I believe that he has submitted it to all of the big journals (Nature, Science, etc.) so you will need access to his Brown e-mail to find out if it is currently under review anywhere else. I will try to find out today from other people in lab who are on the paper and let you know if I get any more information.

Also, just so you know, Damian has started trying to reproduce some of his own data from his Nature Med (2010) paper that everyone in lab is having trouble replicating. I took a look at some of his cell culture flasks yesterday evening and discovered blatant misrepresentation/mislabeling of cell types that are being grown in these flasks, which will drastically alter the results of his experiments and show that he can replicate the data. I immediately took photographs to document my findings and have had two other trusted lab members who are familiar with these experiments look at these flasks themselves so that they can corroborate my findings.

Michael

On Wednesday, April 2, 2014 8:12 AM, "Snyder, Peter" < psnyder@Lifespan.org > wrote: Thanks Michael, for your response. I did not receive any attachment with your last message. Could you kindly re-send that email that you make reference to, to me via either

dropbox or by cutting and pasting into a new message from you? Either way is fine. Please also include the header information for that email.

Also, could you let me know which journals each of the "new" manuscripts are currently under review at, or about to be sent to?

Many thanks,

Dr. Snyder

From: Brown Grad Student [mailto:browngradstudent1@yahoo.com]

Sent: Tuesday, April 01, 2014 4:27 PM

To: Snyder, Peter

Subject: Re: Confidential Update - and a request

Hi Dr. Snyder,

Thank you for contacting General Counsel. Please keep me posted about their suggestions. I will work with Dean Harrington and my department chair to find a new lab. And thank you for offering to help me with this endeavor...I'll let you know if I need your assistance.

Unfortunately, I don't believe I have other e-mails that are pertinent to the investigation. To be honest, I was hoping to keep my qualifying exam issues out of this as much as possible to protect my identity and keep the focus on the published/unpublished papers, which seem to be a much more serious issue. But I will comply if it is critical to the investigation.

The redacted e-mail that I included is the only instance of us ever discussing anything like this via e-mail. As you can see from the e-mail thread where he wrote "The first thing we should do is meet as soon as i return to go over this and decide the best course of action", we met in person when he got back from Spain on 8/21/13. If it would help, I can send you a non-redacted version of this e-mail. I also have the original e-mail from 8/7/13 (there was no text in it, just the attachment) where he sent me a Word document containing an outline for my QE proposal with the potentially fraudulent data "from his former post-doc" that I referred to in the redacted e-mail thread. And then I have the e-mail (again, very little text, just the attachment) where he sent me a PowerPoint file with the "correct" figures at 11:05pm on 8/21/13. Would you like me to send those to you?

In terms of other e-mails, I have a few of the submission/rejection e-mails for the Jorna et al. paper for which I am a co-author. This is the paper where nearly everything was done at Harvard and there is likely no lab notebook for. I can include those if they would help.

FYI, Damian is going to be at a conference in Japan from 4/12 through 4/19.

Michae

On Tuesday, April 1, 2014 2:06 PM, "Snyder, Peter" < <u>psnyder@Lifespan.org</u>> wrote: Hi Michael, I discussed this issue today with the General Counsel for the hospital system, and I am now working with one of his associates – a lawyer that specializes in

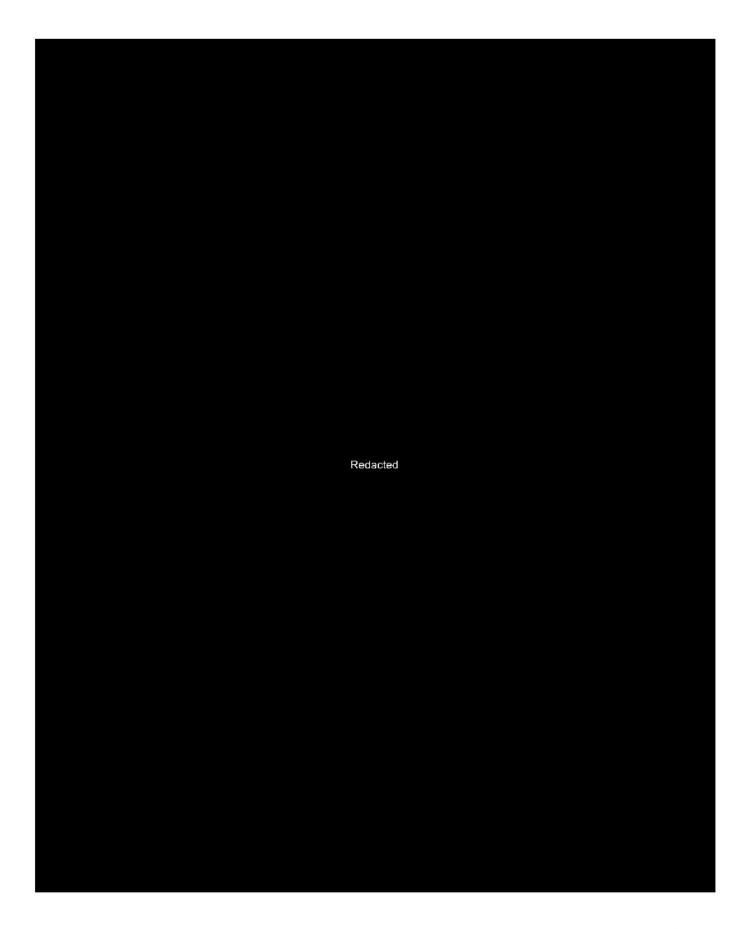
research issues and management. I have worked with her many times before, and she is excellent. I am beginning to consider whom to choose for an 'inquiry committee', and once constituted, that committee will need to meet with you (per our discussion yesterday). Also, I will likely be able to keep this under the radar for about 3-4 weeks, but I may not be able to proceed much farther after that without Dr. Medici being made aware of the investigation. So, it will be very important for you to work with Assoc. Dean Harrington, and with your department chair, to consider alternate laboratories for you to work in over this next month. Again, I will help this along as much as possible — and I would be happy to talk with you about your interests beyond orthopedics and to try to find a good match for you.

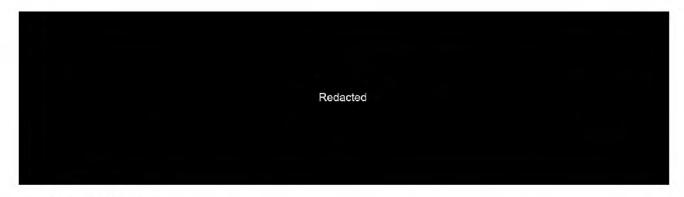
I have one additional request for you at this time. I am sure that you have kept a "paper trail" of emails with Dr. Medici that are pertinent to your concerns. Since he did not use a Lifespan email address, I am unable to retrieve these. Could you please send to me (another Dropbox link would be perfect) ANY emails that you think that I, and the inquiry committee, need to read?? Please include all the header information for each email.

THANKS! Best wishes, Dr. Pete Snyder

Peter J. Snyder, Ph.D.
Sr. Vice President & Chief Research Officer,
Lifespan Hospital System, Providence, RI, U.S.A.
Professor of Neurology,
Alpert Medical School of Brown University
Sr. Associate Editor,
Alzheimer's & Dementia: The Journal of the Alzheimer's Association

Office Telephone: (401) 444-4117 E-Mail: psnyder@lifespan.org





From: Snyder, Peter

Sent: Thursday, April 03, 2014 11:48 AM

To: Sperling, Louis

Cc: Murphy, John B. MD (Administration); Eckford, Therese Flynn; Chupp, Barbara; Snyder, Peter **Subject:** ATTORNEY-CLIENT PRIVILEGE: Suspension of all activity in Medici Lab - Wednesday morning,

09 April

Importance: High

Hi Lou,

Thanks for taking my call today. Since we spoke, the schedule has now changed. Dr. D. Medici will be traveling out of the country (Japan) from the 11th to the 20th, so we will need to move on this before he leaves. Also, I would like to modify the plan regarding what to do with him from an HR perspective, if this is OK with you.

First, can we go up to his lab and close his work at 9am on 09 April? That would be this coming Wednesday. The student in the center of this is aware and is making appropriate plans now. Please let me know if this is possible at your end.

I am empaneling the Inquiry Committee on the morning of the 8th.

The Inquiry Committee has 60 days to complete their work and get their summary to me. I hope it does not take that long, but this will be quite complicated, and they will have to interview at least 4 individuals (and we may want in-house counsel present for 1 or 2 of these) and review lots of visual material.

I would like to recommend the following course of action for Dr. Medici:

- 1) Suspension from all lab activities, and entry onto Coro 4W (with return of lab keys), pending conclusion of this investigation --- and if the Inquiry Committee finds reasonable grounds to pursue, this will go to a 2nd phase.
- 2) No submission of any manuscripts for external peer review without my personal review and authorization

- 3) A halt on all new grant submissions pending completion of the Inquiry Committee's work and my review of their findings
- 4) He may be allowed to continue to manage orthopedics lecture series and to travel to conferences
- 5) Orthopedies can either provide suitable temporary office space for him (not in the Coro Building), or he can work from home.

What is your thought about this suggestion? At this point in time, we are acting prudently on reasonable concerns, but we have no clear determination of fraud at this point.

Thanks.

Peter

Peter J. Snyder, Ph.D.

Sr. Vice President & Chief Research Officer,

Lifespan Hospital System, Providence, RI, U.S.A.

Professor of Neurology,

Alpert Medical School of Brown University

Sr. Associate Editor,

Alzheimer's & Dementia: The Journal of the Alzheimer's Association

Office Telephone: (401) 444-4117

E-Mail: psnyder@lifespan.org



CONFIDENTIAL: Memo to File

09 April, 2014

RE: Dr. D. Medici

This morning, with the assistance of Mr. Lou Sperling, I informed Dr. Damian Medici that he is being placed on suspension from all research-related activities – with pay – to allow the launch of a Research Integrity investigation involving his laboratory and recent publications. In order to proceed with this investigation, and given the reports from one of his graduate students and two research assistants that current experiments in the lab are being conducted in a manner that *may* be designed by Dr. Medici to deliver his expected results, there is a pressing need to close his activities in, and access to, his laboratory at the present time.

The Inquiry Committee will have 60 days to deliver their summary and formulation to my office. In the meantime, we need to do what is reasonably possible to protect Dr. Medici's professional reputation to the extent that this is possible (his lab area is contained within a larger open-lab configuration). I have specifically advised him to let colleagues and students know that he has made a voluntary decision to suspend lab activities for a few weeks or months, to determine why some of his experiments have not been successful as anticipated—and to consider how to correct lab practices that might be adversely impacting his results. So, for the next several weeks or months he will be attending conferences (including a planned overseas conference this month, to Japan I believe), teaching, organizing seminars for the department, and working on papers. This will allow him to remove himself from the lab environment without raising too many questions by peers — especially those external to the Center in the Coro Building.

With regard to his removal from the lab and his employment status, Dr. Medici was informed by myself that – as of this morning – he is:

- Suspended from all lab activities, and barred from entry onto Coro 4W (with return of lab keys), pending conclusion of this investigation --- and if the Inquiry Committee finds reasonable grounds to pursue, this will go to a 2nd phase;
- Prohibited from submitting any manuscripts for external peer review without my personal review and authorization;
- 3) Barred from submission of any new grant applications pending completion of the Inquiry Committee's work and my review of their findings;
- 4) Allowed to continue to manage orthopedics lecture series and to travel to conferences:
- 5) Orthopedics can either provide suitable temporary office space for him (not in the Coro Building), or he can work from home.

Dr. Medici was further instructed to not contact or discuss this investigation, or any facts pertaining to this investigation, with any colleague, student or lab assistant that is, or has been, under his supervision. I specifically informed him that if I receive any information that he has contacted any colleague, student or lab assistant to discuss the specifics of this investigation, or to apply any pressure or intimidation of any type, that this would grounds for immediate dismissal from employment.

I did in form Dr. Medici that the Inquiry Committee is planning to interview him, at great length, and he will have every opportunity to present his understanding of events, and to respond to the concerns being made at this time.

bcc: Mr. Lou Sperling

Dr. John Murphy Dr. Michael Ehrlich Ms. Peggy McGill Copy to file

From: Murphy, John B. MD (Administration)

</o=LSC/ou=LSRESOURCE/cn=Recipients/cn=JMurphy>

To: Snyder, Peter

Sent: 4/8/2014 9:55:43 AM

Subject: RE: CONFIDENTIAL: Service on Research Misconduct Inquiry Committee

Thanks

From: Snyder, Peter

Sent: Tuesday, April 08, 2014 9:36 AM

To: Saab, Carl (carl_saab@brown.edu); Knopik, Valerie (valerie_knopik@brown.edu); Ayala, Alfred;

Michael Carey (michael_carey@brown.edu)

Cc: Snyder, Peter; Murphy, John B. MD (Administration)

Subject: CONFIDENTIAL: Service on Research Misconduct Inquiry Committee

Dear Drs. Saab, Knopik, Ayala and Carey,

I am writing to you in my capacity as the Research Integrity Officer (RIO) for the Lifespan Hospital System, to thank you for agreeing to serve on a very important Inquiry Committee for this institution. As you know, we will be meeting together this morning, and I will provide all relevant information to assist your inquiry and review of a new case involving a faculty member in the Department of Orthopedics, Dr. D. Medici.

With this email, I am asking that you maintain complete confidentiality with regard to all materials, information, interviews and facts pertaining to this case. I have asked Dr. Carl Saab to serve as the Chair for this committee, and Carl has kindly agreed to take on this important responsibility.

I realize that this investigation will require your time, expertise and effort. I want to thank you, on behalf of this hospital system, for your generosity and critically important service.

I will look forward to seeing you in the next hour.

Best,

Peter

Peter J. Snyder, Ph.D.

Sr. Vice President & Chief Research Officer, Lifespan Hospital System, Providence, RI, U.S.A.

Professor of Neurology,

Alpert Medical School of Brown University

Sr. Associate Editor,

Alzheimer's & Dementia: The Journal of the Alzheimer's Association

Office Telephone: (401) 444-4117 E-Mail: psnyder@lifespan.org



Tuesday, April 8, 2014

Lifespan Inquiry Committee_ 1rst meeting

Peter Snyder's charging the committee (10-11:130, Coro Suite 1.009)

- voice recording, transcribing for interviews (Peter's office/Kellie)
- ORI at NIH might be involved in further investigation of federally funded research
- 60 days for final report
- Inquiry Committee shall make recommendations for full panel (hearing)
- M. lab shut down as of Tuesday 9th
- deciding official (John Murphy)
- punitive action: reporting to NIH, dismissal, barred from federal funds, journals
- priorities: protect reputation, safety of the student
- associate dean for graduate students, Beth Harrington, accompanied 3rd year BMI Micheal Susianka, on first visit to submit Allegation
- M. temper "ego, rapid rise in career, great success, lab meetings being arrested at bars, knows where Michael lives, changed his name"
- 2013 produced a qualifying exam requesting figs to support data, M. provided figs and Michael recognized figs were lifted from a prior pub, M. threatened, provided diff figs...
- Eric Darling chair, promotion to associate held out in Dean's office
- 2 papers submitted turned down, rejections, pressure to publish
- failed exps, M. personally performs exps, took stem cells to Harvard, current exps being performed, one assistant told to prepare dish and controlled for experimental set up by withholding cell treatment (analysis pending; suspicion, distrust in lab)
- M. is maintaining outward appearance of continuity, but not allowed to Coro,
 assistants Diana Ramirez/Melissa Ramirez maintain work
- Don Tseng (IACUC) consulted on authenticity of Western
- meeting adjourned (11:30)

MICHAEL SUSIENKA,

1

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EXHIBITS 1-7

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF RHODE ISLAND
C.A. NO. 17-cv-00265-M-PAS

DR. DAMIAN MEDICI,

Plaintiff,

vs

LIFESPAN CORPORATION,
RHODE ISLAND HOSPITAL, and

DEPOSITION of PETER J. SNYDER, Ph.D., a witness called on behalf of the plaintiff, taken pursuant to the applicable provisions of the Federal Rules of Civil Procedure, before Marie C. Leonard, Registered Professional Reporter, Certified Shorthand Reporter No. 146799, and a Notary Public in and for the Commonwealth of Massachusetts, at the offices of Nixon Peabody, One Citizens Plaza, Providence, Rhode Island, on Thursday, February 8, 2018, commencing at 10:10 a.m.

Defendants.

KACZYNSKI REPORTING 72 CHANDLER STREET BOSTON, MA 02116 617.426.6060

1 Α. That's what Dr. Medici is asserting. And there's nothing wrong with that assertion, Ο. 3 correct? MS. WERTHEIMER: Objection. 4 5 I don't know because there have been -- it --Α. 6 it became a repeat pattern. I mean, it's hard to -- it's hard to take away the fact that it happened seven other times. So if this was 9 one instance and if it were me and I thought 10 there was a terrible mistake, maybe my postdoc screwed up, I should figure this out, that 11 12 would be fine. That happens on a rare 13 occasion. But it was -- the next year there 14 were several more instances discovered. That 15 is beyond the pale for a chance -- a rare chance event. And Mr. Susienka over time 16 17 became worried about the repeat pattern. So taking this in isolation is -- is 18 19 very difficult. 20 Ο. Well, did you have any concerns that 21 Mr. Susienka's off balance? 22 MS. WERTHEIMER: Objection. 23 No. He was a skittish graduate student Α. 24 worried about his ability to graduate and have

1 Ο. But you would agree that on a given paper, if 2 an image is incorrect, that if someone's 3 committing misconduct, intentional misconduct, it may be -- it may be one person involved in 4 5 the paper, not all of them; is that a fair 6 statement? MS. WERTHEIMER: Objection. 8 All coauthors are responsible for the content Α. 9 of the paper, but the primary investigator is 10 ultimately responsible for absolutely everything in the paper. 11 12 So you believe a published incorrect image is O. 13 research misconduct by the principal 14 investigator even if a postdoctoral student is the person that was directly involved in that? 15 MS. WERTHEIMER: 16 Objection. There could be an honest mistake; but if it 17 Α. happens on multiple occasions, then it goes 18 19 beyond the -- the realm of possibility that it was a chance of that. 20 21 Okay. But you would agree that for one paper, Ο. 22 one image -- let me strike that. 23 You would agree that research 24 misconduct is intentional misconduct?

- 1 Q. Okay. So I know that you don't recognize this
- document; but it indicates "voice recording,
- 3 transcribing for interviews"?
- 4 A. Yup.
- 5 Q. Now, did you plan on recording all interviews
- 6 during that inquiry?
- 7 A. I asked the inquiry committee to keep records
- 8 and to record them, and I asked my
- 9 administrative assistant to provide the little
- 10 USB Dictaphone device.
- 11 Q. Okay. And part of the inquiry, did you have
- recordings of all interviews?
- 13 A. Yeah. But they were damaged. They were --
- they -- they -- there was a mess.
- 15 Q. And why were they a mess?
- 16 A. I have no idea.
- 17 Q. Were you able to listen to them at all?
- 18 A. They were poor, poor quality. So it was -- we
- 19 were relying -- I think the inquiry -- not me,
- the inquiry committee was relying mostly on
- 21 their own notes from -- from the events. I
- 22 think they had broken transcripts, but it was
- 23 pretty -- pretty poor.
- 24 Q. Do you recall written transcripts ever being

1 written up about the -- the inquiry 2. interviews? 3 For the inquiry interviews, I don't fully Α. 4 recall. I think that there were attempts 5 made, but there were -- there were so many 6 gaps in the audio recordings that they weren't terribly useful. And I think what happened was that my administrative assistant just kept 9 pressing the record button, one after the 10 other; and then when she went later to transcript batches of them, it was discovered 11 12 way too late. 13 Is it your understanding that the recordings O. 14 are still -- that Lifespan still has the 15 recordings? 16 I would doubt that. Α. 17 And why is that? Q. Because these are devices that get overwritten 18 Α. 19 all the time. Do you recall whether it was like a digital 20 Ο. 21 recording or was it like a tape recording? 22 Digital. Α. 23 If you look at this document on page 50, the Ο. 24 fourth one down says, "Inquiry Committee shall

- 1 Q. Okay. But as of the April 8 meeting, he was
- 2 totally unaware of the accusation against him?
- 3 A. I believe that's the case.
- 4 Q. Okay. So prior to his being placed on
- 5 administrative leave, he had no opportunity to
- 6 rebut the charges against him; is that a fair
- 7 statement?
- 8 A. Yes. But he was afforded every opportunity
- 9 after that fact. We had to --
- 10 Q. I'm just --
- 11 A. -- remove him from his lab.
- 12 Q. I understand but just --
- 13 A. Yes.
- 14 Q. Okay. So in the next -- at least a couple
- lines down, it says, "Punitive action:
- Reporting to NIH, dismissal, barred from
- federal funds, journals"; do you see that?
- 18 A. Yes.
- 19 Q. Okay. So your testimony is you didn't say
- that that was going to happen as a result of
- 21 the proceeding; is that a fair statement?
- 22 A. I think what -- my guess from that list is
- 23 that she was -- I must have said something to
- the committee that -- to the effect that any

- 1 -- any -- the results of this inquiry are very
- 2 serious and could dramatically harm
- 3 Dr. Medici's career. So they would have to be
- 4 taken very seriously; and that both the
- 5 respondents and the claimants needed to be
- 6 treated impartially, because the ramifications
- 7 were so serious.
- 8 Q. Who do you think wrote this document?
- 9 A. I believe it was Kellie Najas, who was my
- 10 administrative assistant at the time.
- 11 Q. Does she still work at Lifespan?
- 12 A. Maybe.
- 13 Q. Was she present at the meeting?
- 14 A. I believe I asked her to be there to take
- 15 notes.
- 16 Q. Okay. Who else was present at this meeting?
- 17 A. The committee.
- 18 Q. Okay. And who are the members of the
- 19 committee? There are four, correct?
- 20 A. Yup. Carl Saab, Valerie Knopik, Al Ayala, and
- 21 Michael Carey.
- 22 Q. And you picked all four of them, correct?
- 23 A. I did.
- 24 Q. And what was the basis of -- had any of these

1		committee is simply charged with ascertaining
2		whether there's enough merit to warrant going
3		further. And at that early stage of the
4		investigative process every attempt is made to
5		contain the information in the interest of
6		protecting the integrity after the people
7		involved.
8	Q.	What steps did the inquiry committee take to
9		secure the relevant research data and
10		documents, if you know?
11	A.	Through my office requests were made to
12		receive the laptop computer, access to the
13		hard drive and materials that might inform the
14		case, lab notebooks for which there were none
15		from Dr. Medici, and any source images
16		pertaining to the papers in question.
17	Q.	So is it a fair statement that you, the
18		research integrity officer, took those steps
19		to secure evidence; is that a fair statement?
20	Α.	As best I could at that time.
21	Q.	Why didn't the inquiry committee do that?
22	Α.	Because that's my job is to assist the
23		inquiry committee to facilitate the process.
24		That's the role of the research integrity

1

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EXHIBITS See Index

UNITED STATES DISTRICT COURT FOR THE DISTRICT OF RHODE ISLAND C.A. NO. 17-cv-00265-M-PAS

DR. DAMIAN MEDICI,)

Plaintiff)

vs)

LIFESPAN CORPORATION,)
RHODE ISLAND HOSPITAL, and)
MICHAEL SUSIENKA,)

Defendants

DEPOSITION of CARL SAAB, Ph.D., a witness called on behalf of the plaintiff, taken pursuant to the applicable provisions of the Federal Rules of Civil Procedure, before Barbara J. Vican, Professional Court Reporter, at the offices of Nixon Peabody, One Citizens Plaza, Providence, Rhode Island, on Friday, April 6, 2018, commencing at 1:00 p.m.

KACZYNSKI REPORTING 72 CHANDLER STREET BOSTON, MA 02116

617,426,6060

CARL SAAB, Ph.D.-4/6/18

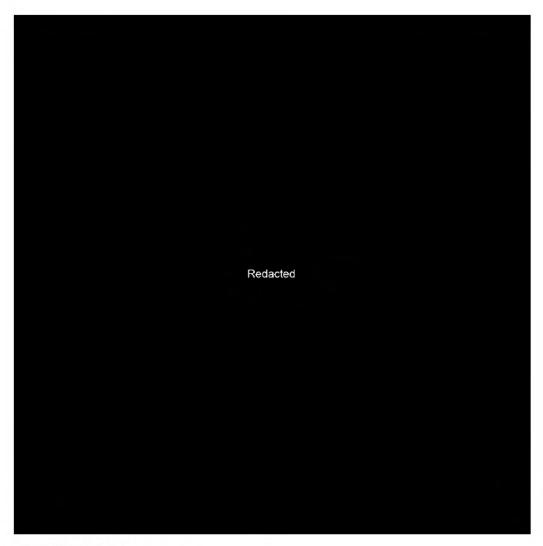
- 1 don't remember he said that. So again, what's
- 2 written in here reflects whatever all of us present
- 3 at the meeting discussed.
- Q. Okay. Where it says, "M lab shut down as
- of Tuesday, the 9th," do you see that?
- 6 A. Mm-hmm.
- 7 Q. And the "M" refers to Medici?
- 8 A. Correct.
- 9 Q. During this meeting, did Dr. Snyder inform
- 10 you that they planned to shut down his lab the next
- 11 day?
- 12 A. It seems to be the case because that was
- 13 April 8th, and April 9th was -- yeah.
- 14 O. Did he indicate that there should be
- 15 punitive action against Dr. Medici?
- 16 A. I don't think so.
- 17 Q. What's your memory as to what you meant
- 18 when you say, "Punitive action: reporting to NIH,
- 19 dismissal, barred from federal funds, journals"?
- 20 A. I think this would mean that in the case
- 21 that if the investigative committee decides that
- there was wrongdoing, that these were some of the
- 23 potential punitive actions that could be taken,
- 24 meaning that we were trying to be careful about how

CARL SAAB, Ph.D.-4/6/18

- 1 we proceed because this might have a huge impact on
- 2 Medici's life and career. So these are some of the
- 3 possible punitive actions that could be taken.
- 4 Q. Okay. So you remember him saying these
- 5 are the possible punitive actions?
- 6 A. Truly, I don't -- that is not what Peter
- 7 said. This is what all the committee discussed.
- Q. Where it says, "Priorities: protect
- 9 reputation, safety of the student, do you see
- 10 that?
- 11 A. Yes.
- 12 Q. Were those the priorities of the
- 13 committee?
- 14 A. Yes.
- 15 Q. What about protection of the respondent's
- 16 reputation? Was that discussed?
- 17 A. Well, everything we were doing in the
- 18 committee was confidential. So it was an
- 19 irrelevant statement.
- 20 Q. Okay.
- 21 A. By virtue of keeping things confidential
- 22 then.
- 23 Q. But you agree that the priorities are
- 24 what's stated next to where it says "priorities"?

CARL SAAB, Ph.D.-4/6/18

- 1 to what we're doing. It depends on who you're
- 2 asking. If you're asking a journal, it would say
- 3 yes. If you're asking an institution, each
- 4 institution has its own policy. If you're asking
- 5 for my opinion, I would say yes.
- 6 Q. All right. I'm just wondering with
- 7 respect to your role in this inquiry committee,
- 8 what standard did you apply with respect to
- 9 Dr. Medici?
- 10 A. It's exactly what I just said, that if
- 11 you're the lead author on a paper and there's
- 12 duplication of facts, not just once, but more than
- once, most likely you are engaged in research
- 14 misconduct. And that was my opinion as chair of
- 15 the committee, which I shared with four other
- 16 committee members, and they shared my opinion.
- 17 Q. Okay. So in your view, at the inquiry
- 18 stage at least, if there is duplicates in two
- 19 papers, that warrants an investigation?
- 20 A. Absolutely.
- 21 (Emails, C. Saab and Brown Grad
- 22 Student, 4/14/14, marked as Exhibit No. 94 for
- 23 identification.)
- Q. Dr. Saab, I'm showing you a document



From: Snyder, Peter

Sent: Tuesday, May 06, 2014 5:18 PM To: Damian Medici@brown.edu

Cc: Snyder, Peter

Subject: CONFIDENTIAL: Preparation for Interview by Investigative Committee

Dr. Medici,

I just met with Dr. Ehrlich, and of course your issues came up in our private conversation. At his request, I would like to state the following:

First, there is a firm 10 day response period, to provide you with an opportunity to provide a written response to the Inquiry Committee report that you received today. I will expect to receive your written response by end-of-business on 16 May. However, this initial response does not prevent or impede you from assembling other materials to assist the Investigative Committee in understanding your position on each of the concerns that have – and will – be raised. Specifically, you are free to assemble materials at your former lab, at Harvard, which

you feel might be important to show the committee. However, the only way any ancillary materials will be of any use, will be if you can prove – with absolute certainty – the origin and provenance of those images, notes, etc... The committee will not be able to use or consider visual, physical or written materials for which the origins can not be **unequivocally** proven. I am not sure what to recommend in this regard, but it may be necessary for you to have relevant materials signed and dated by former colleagues, in the presence of a notary public, with supporting letters that prove their specific provenance.

In the course of this next phase of investigation, you will be interviewed again, and I anticipate that the next interview will require more time, and it will go into greater depth – point by point. You will have ample opportunity to present any and all descriptions, explanations and materials that may support your assertions that there was no research misconduct.

Best,

Peter J. Snyder, Ph.D.

Sr. Vice President & Chief Research Officer,

Lifespan Hospital System, Providence, RI, U.S.A.

Professor of Neurology,

Alpert Medical School of Brown University

Sr. Associate Editor,

Alzheimer's & Dementia: The Journal of the Alzheimer's Association

Office Telephone: (401) 444-4117

E-Mail: psnyder@lifespan.org



This email and any attachment was sent from the law firm Verrill Dana, LLP. It may contain information that is privileged and confidential. If you suspect that you were not intended to receive it, please delete it and notify us as soon as possible. Thank you.

From: Schlissel, Mark <mark schlissel@brown.edu>

To: Snyder, Peter
CC: Savitz, David
Sent: 4/2/2014 8:10:02 PM

Subject: Re: CONFIDENTIAL: Request to conserve e-mail record

From: Schlissel, Mark

Sent: Wednesday, April 02, 2014 08:10 PM

To: Snyder, Peter CC: Savitz, David

Subject: Re: CONFIDENTIAL: Request to conserve e-mail record

Dear Peter,

Done.

Please follow up with the outcome.

best m

Mark Schlissel MD, PhD Provost Professor of Biology Brown University

On Wed, Apr 2, 2014 at 8:54 AM, Snyder, Feter <psnyder@lifespan.org> wrote:

Good morning, Mark,

Yesterday afternoon I spoke briefly to David Savitz, to convey a request to conserve and store the email records for a faculty member in the medical school (Dept. of Orthopedics), Damian Medici, PhD. With this email, I am directing this request to your attention, per David's advice.

Dr. Medici has been employed at Rhode Island Hospital since 2011. Although he is currently an Assistant Professor in Orthopedics at Brown, his laboratory and employment is through RIH. Since arriving in Providence, Dr. Medici has elected to use his Brown Univ. email address, as his primary email, and hence we have very little trace of his email traffic on the Lifespan side. This is the basis for my request to conserve his emails through the university.

Cust recently, a 3rd year graduate student in the Medici lab met with me (accompanied by Assoc. Dean E. Harrington, from the med school) to provide evidence that Dr. Medici may have been creating fraudulent data for submission to peer-review journals, since his employment at RIH. The student provided fairly clear visual evidence (western blots and photomicrographs) that have led me to believe that there may indeed be a factual basis for his claims. In keeping with our institutional policy on Research Misconduct, and in my role as the Research Integrity Officer for the hospital system, I have determined that there is enough concern to warrant an initial 'Inquiry Committee' to be formed so as to further investigate these claims.

This case if further complicated by the fact that the graduate student has specific fears of retaliation from Dr. Medici (including fears of

physical harm), and so I am working now to sequester evidence, empanel the committee, and provide them with documents for review.....for the next 3+ weeks....to allow sufficient time for the graduate student to move out of the Medici lab and to find a new lab to work in for his PhD research (Dr. Harrington and his department chair are working with the student to facilitate this).

So, I am intentionally moving slowly and quietly on this for a few weeks, but I would ask that - as part of this process to protect relevant evidence that the committee may need - that Dr. Medici's emails be protected by Brown and be made available to the Inquiry Committee if and when they make such a request through my office. Many thanks for your consideration of this request, and I look forward

to hearing back at your convenience. Best.

Peter

Peter J. Snyder, Ph.D. Sr. Vice President & Chief Research Officer, Lifespan Hospital System, Providence, RI, U.S.A. Professor of Neurology, Alpert Medical School of Brown University Sr. Associate Editor, Alzheimer's & Dementia: The Journal of the Alzheimer's Association

Office Telephone: (401) 444-4117 <tel: %28401 %29 %20444-4117> E-Mail: psnyder@lifespan.org

----Original Message-----

From: Savitz, David [mailto:david savitz3brown.edu]

Sent: Tuesday, April 01, 2014 7:02 PM

To: Snyder, Peter

Subject: Request to conserve e-mail record

Peter,

I conferred with Jim Green in the Office of the General Counsel who let me know that this type of requested is routed through the Provost. Mark asked for a brief request from you for storing the e-mail of this individual that includes a short note on your view of what provides a sufficient basis for going forward with a full hearing. With that, he will request that CIS take the necessary action to store the e-mail files. Let me know if you'd like to discuss further. Thanks. David

David A. Savitz, PhD Vice President for Research Professor of Epidemiology Professor of Obstetrics and Gynecology Brown University Box 1937 (Interoffice mail) 47 George Street, 3rd Floor, Room 302 Providence, RI 02912 (401) 863-7408 (office)

(401) 863-9994 (fax)

E-mail: david_savitz@brown.edu

From: Carl Saab <carl_saab@brown.edu>

To: Medici, Damian

CC: Damian_Medici@brown.edu; Snyder, Peter; michael_carey@brown.edu;

Ayala, Alfred; Valerie Knopik

Sent: 4/11/2014 10:55:42 AM

Subject: CONFIDENTIAL_Request for Interview

Dr. Medici,

My name is Carl Saab and I am chair of an Inquiry Committee at Lifespan, set up by Dr. Peter Snyder. The committee is tasked with fact-finding regarding Allegations of Research Misconduct in your laboratory. For more information about Lifespan's Policy on Research Misconduct, including our committee's tasks, please refer to attached document.

It is very important that we meet with you for an Interview on <u>Monday, April 21, 10:30-12:00, Coro West, Suite 1.009</u>.

During the interview, you should expect to hear questions regarding experimental protocols and data produced in your laboratory. You are encouraged to bring your personal laboratory notebook, as well as other material evidence you wish to share with the committee.

Please confirm that you have received this email and that you will be present for the interview.

Regards, Carl.

EXHIBIT B

CONFIDENTIAL: Attorney - Client Privilege

To:
Peter Snyder, PhD
Lifespan SVP & Research Integrity Officer
Monday, April 28, 2014

Lifespan Inquiry Committee Summary Report

Allegations of Research Misconduct in Dr. Damian Medici's laboratory

This is the Inquiry Committee's (IC) **Summary Report** including preliminary evaluation of images, published articles, submitted manuscripts, laboratory notebooks, as well as recorded and transcribed interviews with various laboratory staff and students, all working under the direct supervision of Dr. Damian Medici (Department of Orthopedics). The IC has determined there is **sufficient evidence** warranting further **Investigation** of possible Research Misconduct.

Lifespan's Inquiry Committee (IC):

The committee was made up of four Lifespan employees: Valeric Knopik, PhD; Michael Carey, PhD, Alfred Ayala, PhD and Carl Saab, PhD (IC chair). The IC is an ad-hoc committee that was formed by Dr. Peter Snyder, Lifespan's Research Integrity Officer, who then submitted charges to the IC on 4/8/ 4@ 10:00 describing potential Allegations of Research Misconduct in Dr. Damian Medici's Jaboratory.

Interview schedules:

After careful consideration of the initial Allegations, IC moved promptly to interview the following members of the Medici lab at the following dates/places: Michael Susienta (Graduate student, 4/11/14, 8:30-9:50, RIH, Coro West 1.009); Melissa Ramirez (Lab assistant, 4/17/14, 9:00-10:50, RIH, Aldrich 402); Olin Liang (Instructor, 4/17/14, 11:00-11:30, RIH, Aldrich 402); Diana Ramirez (Lab assistant, 4/18/14, 9:00-9:50, RIH, Aldrich 402); Dam.an Medici (PI, 4/21/14, 10:30-11:40, Coro West 1.309).

Interview process:

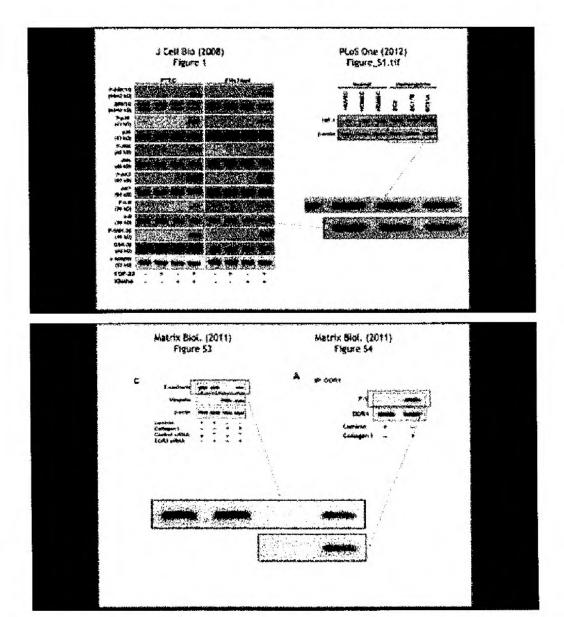
All those contacted responded promptly to the request for interview by IC. All interviews were voice-recorded (transcriptions made available only to Dr. Snyder) after obtaining approval from Interviewees (signed forms attached). Interviewees also received a print copy of Lifespan's updated Research Misconduct Policy. At all times, IC members made every possible effort to be objective, impartial and fair, while prioritizing protection of the Respondent's reputation and anonymity of the Complainant(s).

Evidence reviewed:

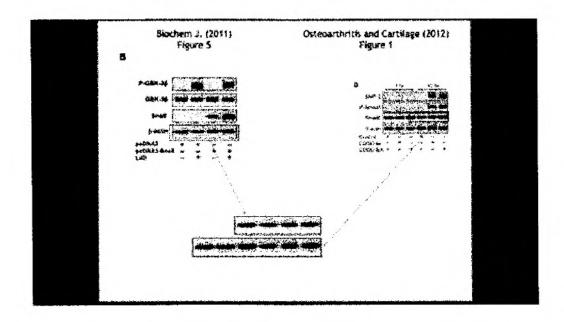
Prior to the interviews, the IC examined closely all evidence related to the initial allegation. Of note, per Lifespan policy, the inquiry "does not require full review of all the evidence related to the initial allegation". Therefore, IC members identified a series of allegations which, in the opinion of the committee, amounted to 'strong and credible evidence' for potential Research Misconduct. These allegations suggested duplication of the same figures in multiple manuscripts,

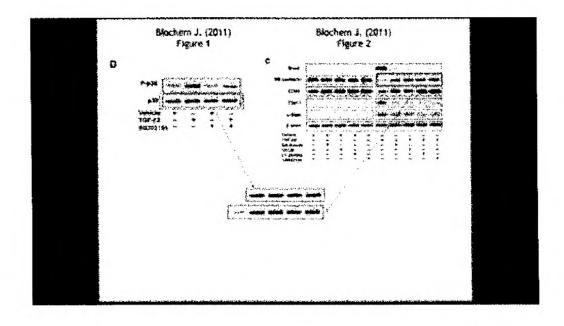
INQUIRY COMMITTEE/SUMMARY REPORT

describing in each case a different data set (see figures below). If confirmed, this would amount to Fabrication/Falsification of data in published manuscripts, as well as in copies of manuscripts submitted, during Dr. Medici's employment by this institution, for publication and/or under revision (heretofore referred to as 'pending'; electronic copies submitted to the committee).

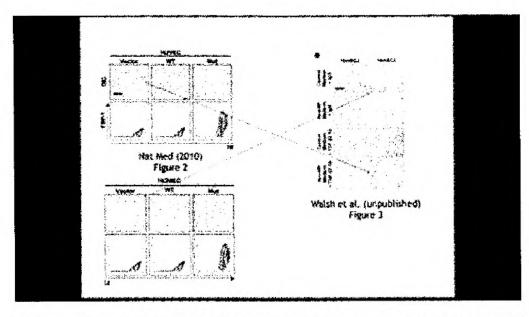


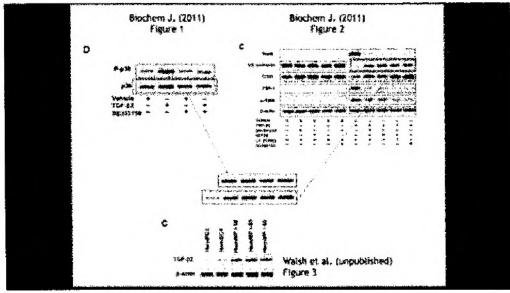
INQUIRY COMMITTEE/SUMMARY REPORT





INQUIRY COMMITTEE/SUMMARY REPORT





Interview strategy:

Based on the evidence, the IC focused on cross-referencing these figures (see above) in published manuscripts and identifying the source(s) of these data. Therefore, Interviewees were asked specific questions related to general research environment in the lab, as well as detailed scientific questions, technical experimental protocols, lab notebooks, and preliminary data.

Summary of interviews:

In sum, interviews (entire transcripts of each interview will be submitted to Dr. Snyder, for future reference and use by a possible Investigative Committee) revealed a general lab environment in which the PI (Dr. Medici) oversees work in the lab, mainly via regular lab meetings (usually on Tuesdays). No major complaint was noted regarding personal interactions in the lab. However, throughout the course of these interviews, the IC became concerned that members of the Medici lab, listed as co-authors on pending manuscripts, were given hard-copies only for the purpose of writing down comments and editorial feedback to Dr. Medici prior to first submission, instead of electronic copies. These co-authors were not involved during subsequent submissions of the same manuscript(s). As a result, some of the data generated in the Medici lab, which were included in unpublished versions of 'pending' manuscripts, remain of untraceable origins to the IC (e.g. Walsh et al. unpublished Fig 3, see above). Moreover, the IC is concerned for the lack of 'book-keeping' in the lab. Apparently, lab members are not encouraged to keep personal notebooks. Only Diana and Melissa use standard lab notebooks with annotations and signatures, primarily because they were trained to do so at a previous institution (Melissa's lab notebooks were secured by IC). This concern became significant when the IC was trying to trace the source of generated data that are represented in some of the figures above, in particular those related to pending manuscript by Walsh et al.

During the IC's interview, Dr. Medici expressed 'shock' at the allegations, while acknowledging strong 'similarities' in the figures shown to him and expressing a deep sense of 'regret' for these 'mistakes'. At the same time, the source of these figures remains undetermined (Dr. Medici could not explain). The use of similar blots and/or micrographs, if proven to be exact replica, would constitute research misconduct for work performed onsite at Lifespan and under the direct supervision of Dr. Medici (at least for Walsh et al. Fig 3, see above).

One concern raised by the lab group relates to lack of success – by all junior lab members (i.e., Diana, Melissa and Michael) – in their many attempts to replicate previously published data by Dr. Medici (Medici et al. Nat Med 2010). They were trying to replicate the "conversion of dermal vascular endothelial cells into multipotent stem-like cells", a central claim made by the authors in that manuscript. The testimony by the lab members was consistent, namely, that Dr. Medici was involved in resolving this issue by personally performing a set of experiments in the lab, with the aim of achieving cell conversion, as recently as April 2014; however, their consistent testimonies conflict with Dr. Medici's statement that he did not perform his experiments in the lab, and 'stepped in' only occasionally to help others with their experiments. Reconciling this inconsistency is difficult in the absence of written documentation on the part of Dr. Medici (he does not keep a lab notebook). Therefore, the IC strongly recommends a deeper look into concerns related to on-going research activities in the Medici lab, particularly as of April 2014, aimed at reproducing data published by Medici et al. Nat Med 2010.

Conclusions of the inquiry and recommendation:

Based on the above, the IC concluded that there is a reasonable basis for the allegation (even if just restricted to figures provided above), which appears to have substance and falls within the definition of Research Misconduct relative to data/image fabrication/falsification.

Accordingly, the IC recommends further Investigation into this allegation.

Sincerely,		
	Monda); April 2	8, 2614
Alfred Ayala, PhD	Michael Carcy, PhD	
Carl Saab, PhD (IC chair)	Valerie Knopik, PhD	
INQUIRY COMMITTEE/SUMMARY REPORT		P7



Corrina L. Hale E-mail: chale@toddweld.com

October 3, 2014

BY FIRST CLASS MAIL & E-MAIL

Kate Gallin Heffernan, Esq. Verrill Dana LLP One Boston Place Suite 1600 Boston, MA 02108-4427

Re: Dr. Damian Medici

Dear Attorney Heffernan:

I write in response to your September 29 and October 1 e-mails requesting that Dr. Medici produce documents to Lifespan.

Lifespan's requests are untimely, unfair and appear calculated to create a false impression that Dr. Medici is somehow unwilling or unable to provide information in this process. For example, you are personally fully aware that months ago we participated in a meeting at which we requested on Dr. Medici's behalf that Lifespan work with us constructively so that materials known or believed to be located at Harvard which are critical to this process could be obtained. Lifespan not only declined our invitation but it then reported the matter to Harvard, without notice to or input from Dr. Medici, in a manner which both acknowledges the impropriety of Lifespan's attempting to make certain matters part of this "process" in the first place, and which makes it impossible for Dr. Medici to obtain materials from that source. It is hard to conceive of a more vindictive and unfair request for Lifespan to now ask Dr. Medici, on one week's notice, to provide source materials it knows he cannot obtain.

To the extent that Lifespan's untimely requests relate to materials sequestered by Lifespan itself and to which Lifespan has denied Dr. Medici any access, its request is even more absurd and in bad faith. Put simply, Lifespan seized materials from Dr. Medici's lab, refused to give him access to those materials so he can defend himself, and now asks him to produce documents from those materials in advance of his interview. This is improper.

Dr. Medici will bring with him to his interview any materials he has been able to access on his own given the improper limitations which have been imposed upon him, and based upon which he relies to disprove the false accusations made against him. Given Lifespan's actions to date, those materials will necessarily be limited, and unfairly so.



October 3, 2014 Page 2 of 3

I should further note with respect to the growing basic unfairness of this process, that we are deeply concerned that Lifespan appears to have destroyed evidence in this case. According to the April 28th Inquiry Report, the interviews with Dr. Medici and his lab members, Michael Susienka, Diana Ramirez, Melissa Ramirez, and Olin Liang, were voice-recorded and transcribed, and all of the transcriptions were made available to Dr. Snyder. As you know, we requested a copy of the tape or transcript of Dr. Medici's interview in late June (or early July) of 2014, and we have heard numerous explanations from Lifespan since then about its purported inability to produce any transcript. When we finally received a copy of the tape recording of that one interview, the quality was so poor that the tape is essentially useless. We have been denied any access at all to these other interviews.

Dr. Medici, through counsel, hereby repeats his demand that Lifespan immediately produce to us a copy of the transcription of his interview that was provided to Dr. Snyder, along with the transcriptions of the interviews of Michael Susienka, Diana Ramirez, Melissa Ramirez, and Olin Liang, and that Dr. Medici be given a fair opportunity to review those transcripts before any interview of him takes place.

In this regard, please note that the Lifespan Policy specifically states that, even as early as the inquiry phase, "[s]upervised access to the data and/or documents should be available to the Respondent." See Lifespan Policy, at §IV.C. The Lifespan Policy specifies that it is the Respondent (not solely his attorneys) who should have access to the materials. Id. I suspect you know that the Lifespan Policy does not state that the Respondent's access ends at any particular time. On August 7, 2014, Dr. Medici, through counsel, made a request to see all of the lab notebooks and materials collected from his lab. Lifespan denied Dr. Medici's request and has refused to permit him to review any of the evidence in its possession in advance of his upcoming interview. Lifespan's offer to allow me or Howard Cooper "supervised access to the laboratory notebooks of other [lab] members" (but not to Dr. Medici's notes and computer files) is no substitute. We believe that Lifespan is intentionally interfering with Dr. Medici's ability to defend himself in this matter,

Dr. Medici, through counsel, hereby demands that Lifespan immediately produce to us a copy of all documents and things that Lifespan collected from his lab, including, but not limited to, lab notebooks and notes, computer hard drives, data, images, figures, manuscripts, and all other materials. Dr. Medici also demands that Lifespan produce to us a copy of all of the materials that the Lifespan Inquiry Committee, Lifespan Investigation Committee, and/or Dr. Snyder reviewed in relation to these proceedings, including, but not limited to, transcriptions of all interviews. We will, of course, enter into an appropriate protective order so that no materials are misused in any fashion.



October 3, 2014 Page 3 of 3

Assuming that Lifespan remains unwilling to produce materials as we have requested and as part of a fair process, we ask you to please confirm that the Investigation Committee will meet with Dr. Medici on Tuesday, October 7 from 11:30am-1:30pm, and provide the location of the meeting. Please be advised that we will be bringing a court reporter to Dr. Medici's interview.

Corrina L. Hale

CLH/af

cc: Therese Flynn Eckford, Esq. Kenneth E. Arnold, Esq. Peter Snyder, PhD Howard M. Cooper, Esq. Dr. Damian Medici (all via email only)



Lifespan

PERSONAL & CONFIDENTIAL

06 May, 2014

Damian Medici, Ph.D. 790 Boylston Street, Apt. 18J Boston, MA 02199

RE: Lifespan Hospital System Investigation of Possible Research Misconduct

Dear Dr. Medici.

Enclosed, please find a copy of the report of the Inquiry Committee that I had formed to explore initial allegations and concerns of research misconduct within your laboratory. The purpose of this committee was to rapidly review a subset of documentation, images, laboratory notebooks, and to conduct appropriate interviews – all with the sole purpose of recommending whether or not a more complete investigation is warranted.

As a result of this committee's review of records and deliberations, they have recommended that a formal investigation be launched, and I have accepted their advice. Per our institutional policy on research conduct, provided to you previously, I will select faculty members to form a new Investigative Committee.

The next steps will be as follows:

- 1) You will have 10 days from the receipt of this letter (sent by private courier with signature required) to prepare and to submit a written response to the enclosed Inquiry Committee report. Your response will be attached as an addendum to the report, and it will be provided to the Investigative Committee for their review and consideration;
- 2) Ten days after your receipt of this letter and/or once I receive your written response (please send it either by e-mail or, if you prefer, by standard mail to my mailing address provided below), I will formally launch the Investigative Committee. This new committee will have 120 days, maximum, to complete their work and to deliver a final report to my office.
- 3) In addition, at the present time I am mandated, by Federal regulations and by our Institutional Policy, to notify the NIH Office of Research Integrity that this investigation is taking place (and I am required to provide a listing of your current Federal grants).

You may be contacted by Lifespan's Human Resources Department regarding your current employment status.

Peter J. Snyder, PhD Senior Vice President and Chief Research Officer

Research Administration Coro West One Hoppin Street 1st Floor, Suite 1.001 Providence, RI 02903

Tel 401 444-4117 Email psnyder@lifespan.org

Professor Department of Neurology The Warren Alpert Medical School of Brown University

Adjunct Professor Child Study Center Yale University School of Medicine

Senior Associate Editor, Alzheimer's & Dementia: The Journal of the Alzheimer's Association



Finally, with this letter, I am reminding you that it would be entirely unacceptable for you to contact ANY member of your laboratory group, including employees and students, for any reason. If you do contact any individual connected with your laboratory, by e-mail, text messages, telephone or in person, I will consider such an act to reflect tampering with this investigative process, and you will both be immediately dismissed from employment and your NIH funding will be terminated.

You will be asked to appear before the Investigative Committee, and the chair of that committee will be contacting you in due course.

Thank you,

Peter J. Snyder, Ph.D.

Sr. Vice President & Chief Research Officer,

Planton

Research Integrity Officer,

Lifespan Hospital System, Providence, RI, U.S.A.

Professor of Neurology,

Alpert Medical School of Brown University

Sr. Associate Editor,

Alzheimer's & Dementia: The Journal of the Alzheimer's Association

Office Telephone: (401) 444-4117 E-Mail: psnyder@lifespan.org

Mailing Address:
Office of the Chief Research Officer
Lifespan Hospital System
1 Hoppin Street, Suite 1.001 (Coro West)
Providence, RI 02903

cc: Barbara Chupp, Esq. M. Ehrlich, M.D. copy to file

From: Snyder, Peter

</O=LSC/OU=LSRESOURCE/CN=RECIPIENTS/CN=PSNYDER>

To: Murphy, John B. MD (Administration)

Sent: 5/19/2014 12:08:28 PM

Subject: Attorney-Client Privilege: Medici Response to inquiry committee

Hi John,

Attached, please find the original Inquiry Report (previously sent) and the responses from Dr. Medici. We are meeting on Wednesday morning, with Dr. Ehrlich, to discuss. I will try to reach you by telephone in advance of that meeting.

Thanks, Peter

From: Medici, Damian [mailto:damian_medici@brown.edu]

Sent: Friday, May 16, 2014 4:57 PM

To: Snyder, Peter; dmeier@toddweld.com; hcooper@toddweld.com

Subject: Response to inquiry committee

Dear Dr. Snyder,

Please find attached my response to the Inquiry Committee Report. I have also attached a copy of the letter that I emailed to the Inquiry Committee on April 25, 2014. I am not sure whether you have seen the letter.

I also want to mention that it has been brought to my attention that the confidentiality of your investigation has been breached both inside and outside of Lifespan. These false and inaccurate allegations and the lack of confidentiality in the inquiry process have already done significant damage to my reputation and career. Therefore, I have sought legal counsel and I have cc'd this email to my attorneys, David Meier and Howard Cooper of Todd & Weld LLP in Boston, Massachusetts.

I ask that you please read the attached documents carefully prior to taking any further action, and if you choose to proceed any further with your investigation, to please make these documents immediately available to the Committee.

I also ask that you and anyone else associated with this matter please include my attorneys in all future correspondence until this issue is resolved.

Kind regards,

Dr. Damian Medici

From: Valerie Knopik <valerie knopik@brown.edu>

To: Michael Carey

CC: Snyder, Peter; Carl Saab; Ayala, Alfred; Eckford, Therese Flynn

Sent: 5/21/2014 7:13:34 PM

Subject: Re: Attorney-Client Privilege: Message to Inquiry Committee

All,

I apologize for the delay. I needed to find a chunk of time to read and reflect on Dr Medici's letter. I agree with the rest of the committee and support our initial decision that a more thorough investigation is needed. \hat{A}

Sincerely, Valerie

Sent from my iPhone

On May 21, 2014, at 5:56 PM, Michael Carey < michael carey@brown.edu > wrote:

Hello Peter,

I have reviewed Dr. Medici's letter carefully. Â After reviewing it, I continue to believe that a more thorough investigation is warranted, consistent with the recommendation made by the Inquiry Committee in our Report to you. Given the gravity of the allegations, a thorough investigation is needed. Â Dr. Medici will have the opportunity to respond to the allegations as part of a more detailed investigation.

Sincerely, A

Mike

Michael P. Carey, PhD

Director, Centers for Behavioral and Preventive Medicine

On May 21, 2014, at 3:21 PM, Snyder, Peter < psnyder@Lifespan.org > wrote:

Dear Carl, Al, Valerie and Mike,

Â

Enclosed please find Dr. Medici's comments to the report your Inquiry Committee submitted to me on April 28, 2014. Lifespan is in the process of finalizing its mandatory reporting of this matter to the Office of Research Integrity. Please review Dr. Medici's comments at your earliest convenience (preferably today) and confirm to me whether there is anything in these comments that would change your recommendation, stated in the Inquiry Committee Report, that Lifespan should pursue further investigation of this matter.

Â

Thanks very much,

```
Peter Â
Peter J. Snyder, Ph.D.
Sr. Vice President & Chief Research Officer,
 Lifespan Hospital System, Providence, RI, U.S.A.
Professor of Neurology,
 Alpert Medical School of Brown University
Sr. Associate Editor,
 Â Alzheimer's & Dementia: The Journal of the Alzheimer's Association
Â
Office Telephone:Â (401) 444-4117
E-Mail:Â psnyder@lifespan.org
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<Response to Inquiry Committee.pdf>
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From: Snyder, Peter

</O=LSC/OU=LSRESOURCE/CN=RECIPIENTS/CN=PSNYDER>

To: 'Carl Saab'

CC: Ayala, Alfred; valerie_knopik@brown.edu; michael_carey@brown.edu;

Eckford, Therese Flynn

Sent: 5/21/2014 4:06:20 PM

Subject: RE: Attorney-Client Privilege: Message to Inquiry Committee

Thank you, Carl.

We will wait to hear from Al, Mike and Valerie as well.

Peter

From: Carl Saab [mailto:carl_saab@brown.edu] Sent: Wednesday, May 21, 2014 3:57 PM

To: Snyder, Peter

Cc: Ayala, Alfred; valerie knopik@brown.edu; michael carey@brown.edu; Eckford, Therese Flynn

Subject: Re: Attorney-Client Privilege: Message to Inquiry Committee

Importance: High

Dear Peter.

Dr. Medici's comments (attached to your letter) do *not* make me want to change my recommendation.

Best,

Carl.

On May 21, 2014, at 3:21 PM, Snyder, Peter <psnyder@Lifespan.org> wrote:

Dear Carl, Al, Valerie and Mike,

Enclosed please find Dr. Medici's comments to the report your Inquiry Committee submitted to me on April 28, 2014. Lifespan is in the process of finalizing its mandatory reporting of this matter to the Office of Research Integrity. Please review Dr. Medici's comments at your earliest convenience (preferably today) and confirm to me whether there is anything in these comments that would change your recommendation, stated in the Inquiry Committee Report, that Lifespan should pursue further investigation of this matter.

Thanks very much, Peter

Peter J. Snyder, Ph.D. Sr. Vice President & Chief Research Officer, Lifespan Hospital System, Providence, RI, U.S.A. Professor of Neurology, Alpert Medical School of Brown University Sr. Associate Editor,

Alzheimer's & Dementia: The Journal of the Alzheimer's Association

Office Telephone: (401) 444-4117 E-Mail: psnyder@lifespan.org <image001.gif>

<Response to Inquiry Committee.pdf>

From: Snyder, Peter

</O=LSC/OU=LSRESOURCE/CN=RECIPIENTS/CN=PSNYDER>

To: Murphy, John B. MD (Administration)

CC: Eckford, Therese Flynn; Arnold, Kenneth - Legal Dept; Snyder, Peter

Sent: 5/20/2014 1:55:36 PM

Subject: Attorney-Client Privilege: Res. Misconduct Case

Dear John,

As you know, I met today – in confidence – with Dr. Jack Wands, and I asked for his professional opinion and judgment with respect to his independent review of the photographic case materials regarding the Medici lab. He was unequivocal in his belief that there is sufficient reason to suspect research misconduct, and his recommendation is to allow this investigation to move forward into the next phase. Dr. Wands opinion is in direct support of a separate and independent opinion reached by two other senior researchers in our hospital system – all in addition to the summary impression of the 4 members of the Inquiry Committee.

With a heavy heart, and with trepidation, I have no choice but to recommend to you – as the Deciding Official for this institution – that we both report this case officially to the Office of Research Integrity of the NIH, as well as to empanel a new Investigative Committee (we discussed the members of this new committee, this morning). I am confident that this new committee will conduct a thorough, fair, impartial investigation, and that it will render a summary judgment that is defensible and appropriate. Our in-house counsel, Therese Eckford, Esq., is currently editing the draft cover letter that we will need to send all materials to ORI. I am recommending that we send these materials, and start a 120 day clock for the next phase of this investigation, on Thursday of this week (22 May, 2014). I am confident that the Investigative Committee will not require this full amount of time to complete their work.

Peter J. Snyder, Ph.D.
Sr. Vice President & Chief Research Officer,
Lifespan Hospital System, Providence, RI, U.S.A.
Professor of Neurology,
Alpert Medical School of Brown University
Sr. Associate Editor,
Alzheimer's & Dementia: The Journal of the Alzheimer's Association

Office Telephone: (401) 444-4117 E-Mail: psnyder@lifespan.org

